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=> d stat que

L1          164 SEA FILE=REGISTRY HPV?
L2          872 SEA FILE=REGISTRY PROTEIN E?/CN
L3           74 SEA FILE=REGISTRY "PROTEIN L1"?/CN
L4       172330 SEA FILE=HCAPLUS L1 OR HPV? OR PAPILLOMA?
L5         1659 SEA FILE=HCAPLUS PROTEIN(W)E OR L2
L6          910 SEA FILE=HCAPLUS "PROTEIN L1"? OR L3
L8           19 SEA FILE=HCAPLUS L5 AND L6
L9            5 SEA FILE=HCAPLUS L4 AND L8


=> d ibib abs hitrn l9 1-5


L9   ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        2000:557272  HCAPLUS
DOCUMENT NUMBER:         134:25996
TITLE:                   Distinct patterns of alteration of myc genes
                         associated with integration of human
                       papillomavirus type 16 or type 45 DNA in two
                         genital tumours
AUTHOR(S):               Sastre-Garau, Xavier; Favre, Michel; Couturier,
                         Jerome; Orth, Gerard
CORPORATE SOURCE:        Unite Mixte Institut Pasteur/INSERM (U.190), Institut
                         Pasteur, Paris, F-75724, Fr.
SOURCE:                  J. Gen. Virol. (2000), 81(8), 1983-1993
```

CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We previously described two genital carcinomas (IC2, IC4) contg. human **papillomavirus** type 16 (**HPV**-16)- or **HPV**-18-related sequences integrated in chromosomal bands contg. the c-myc (8q24) or N-myc (2p24) gene, resp. The c-myc gene was rearranged and amplified in IC2 cells without evidence of overexpression. The N-myc gene was amplified and highly transcribed in IC4 cells. Here, the sequence of an 8039 bp IC4 DNA fragment contg. the integrated viral sequences and the cellular junctions is reported. A 3948 bp segment of the genome of **HPV**-45 encompassing the upstream regulatory region and the E6 and E7 ORFs was integrated into the untranslated part of N-myc exon 3, upstream of the N-myc polyadenylation signal. Both N-myc and **HPV**-45 sequences were amplified 10- to 20-fold. The 3' ends of the major N-myc transcript were mapped upstream of the 5' junction. A minor N-myc/**HPV**-45 fusion transcript was also identified, as well as two abundant transcripts from the **HPV**-45 E6-E7 region. Large amts. of N-myc protein were detected in IC4 cells. A major alteration of c-myc sequences in IC2 cells involved the insertion of a non-coding sequence into the second intron and their co-amplification with the third exon, without any evidence for the integration of **HPV**-16 sequences within or close to the gene. Different patterns of myc gene alterations may thus be assocd. with integration of **HPV** DNA in genital tumors, including the activation of the protooncogene via a mechanism of insertional mutagenesis and/or gene amplification.

IT **312330-91-9 312330-92-0 312330-93-1 312330-94-2 312330-95-3**
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(amino acid sequence; distinct patterns of alteration of myc genes assocd. with integration of human **papillomavirus** type 16 or type 45 DNA in two genital tumors)

IT **190691-38-4**, GenBank Y13218 **273186-28-0**, GenBank AJ242956
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; distinct patterns of alteration of myc genes assocd. with integration of human **papillomavirus** type 16 or type 45 DNA in two genital tumors)

REFERENCE COUNT: 55
REFERENCE(S):
(6) Choo, K; Cancer Letters 1995, V93, P249 HCAPLUS
(7) Coombs, L; Analytical Biochemistry 1990, V188, P338 HCAPLUS
(8) Couturier, J; Journal of Virology 1991, V65, P4534 HCAPLUS
(9) Cullen, A; Journal of Virology 1991, V65, P606 HCAPLUS
(10) Daniel, B; Journal of General Virology 1997, V78, P1095 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:224575 HCAPLUS
DOCUMENT NUMBER: 133:85001

TITLE: Rabbit Oral **Papillomavirus** Complete Genome Sequence and Immunity Following Genital Infection
AUTHOR(S): Christensen, Neil D.; Cladel, Nancy M.; Reed, Cynthia A.; Han, Ricai
CORPORATE SOURCE: Department of Pathology, The Milton S. Hershey Medical Center, Penn State College of Medicine, Hershey, PA, 17033, USA
SOURCE: Virology (2000), 269(2), 451-461
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rabbit oral **papillomavirus** (ROPV) infects mucosal tissues of domestic rabbits. The viral genomic sequence has been detd. and the most related **papillomavirus** type was the cutaneous cottontail rabbit **papillomavirus** (CRPV). Homologies between the open reading frames (ORFs) of ROPV and CRPV, however, ranged from 68% amino acid identity for L1 to only 23% identity for E4. Shared features unique to the two rabbit viruses included a large E6 ORF and a small E8 ORF that overlapped the E6 ORF. Serol. responses to ROPV L1 viruslike particles (VLPs) were detected in rabbits infected at either the genital or oral mucosa with ROPV. The antibody response was specific to intact ROPV L1 VLP antigen, was first detected at the time of late regression, and persisted at high levels for several months after complete regression. Both oral and genital lesions regressed spontaneously, accompanied by a heavy infiltrate of lymphocytes. ROPV infection of rabbit genital mucosa is a useful model to study host immunol. responses to genital **papillomavirus** infections. (c) 2000 Academic Press.

IT **280785-91-3**, Protein E6 (Rabbit oral **papilloma** virus)
280785-93-5, Protein E1 (Rabbit oral **papilloma** virus)
280785-95-7, Protein E4 (Rabbit oral **papilloma** virus)
280785-96-8, Protein E5 (Rabbit oral **papilloma** virus)
280785-98-0, **Protein L1** (Rabbit oral **papilloma** virus) **281200-68-8**, Protein E8 (Rabbit oral **papilloma** virus)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; rabbit oral **papillomavirus** complete genome sequence and immunity following genital infection)

REFERENCE COUNT: 28
REFERENCE(S):
(1) Barbosa, M; J Virol 1987, V61, P2938 HCAPLUS
(2) Bernard, H; Curr Top Microbiol Immunol 1994, V186, P33 HCAPLUS
(3) Christensen, N; J Gen Virol 1994, V75, P2271 HCAPLUS
(4) Christensen, N; J Gen Virol 1996, V77, P1793 HCAPLUS
(6) Christensen, N; Virology 1996, V223, P174 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:674801 HCAPLUS
DOCUMENT NUMBER: 123:189703
TITLE: Nucleotide sequence of a canine oral **papillomavirus** containing a long noncoding region

AUTHOR(S): Isegawa, Naohisa; Ohta, Mitsuhiro; Shirasawa, Hiroshi; Tokita, Hisashi; Yamaura, Akira; Simizu, Bunsiti
CORPORATE SOURCE: School of Medicine, Chiba University, Chiba, 260, Japan
SOURCE: Int. J. Oncol. (1995), 7(1), 155-9
CODEN: IJONES; ISSN: 1019-6439
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The DNA genome of a canine oral **papillomavirus** (COPV) was completely sequenced and found to consist of 8607 base pairs, which were the longest of all known **papillomaviruses** (PVs). Its organization was similar to that of other PVs except that it lacked early gene 5 (E5) and possessed a unique long noncoding region (L-NCR) between the end of the early genes and the beginning of the late genes. COPV also possessed a short noncoding region (S-NCR) which contained a putative upper regulatory region (URR), which is commonly found in PVs. The L-NCR did not show any similarity to known PV DNAs nor other DNA sequences in the GenBank database. Nucleotide sequence anal. of COPV showed that it was closely related to human **papillomavirus** type 1 (**HPV** 1) and animal PVs assocd. with cutaneous lesions in rabbit, European elk, deer and cow as we reported previously.

IT **158888-99-4 158889-00-0 158889-01-1 158889-02-2 158889-05-5**
RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; complete sequence of canine oral **papillomavirus**, contains a long noncoding region)

L9 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:628556 HCAPLUS
DOCUMENT NUMBER: 123:219701
TITLE: Sequence determination of human **papillomavirus** type 6a and assembly of virus-like particles in Saccharomyces cerevisiae
AUTHOR(S): Hofmann, Kathryn J.; Cook, James C.; Joyce, Joseph G.; Brown, Darron R.; Schultz, Loren D.; George, Hugh A.; Rosolowsky, Mark; Fife, Kenneth H.; Jansen, Kathrin U.
CORPORATE SOURCE: Department of Virus and Cell Biology, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Virology (1995), 209(2), 506-18
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human **papillomavirus** 6a (**HPV6a**), the most abundant **HPV6** subtype, was detected in a vulvar condyloma acuminatum. The complete genome of **HPV6a** was cloned, and its DNA sequence was shown to be >97% identical to the **HPV6b** sequence. Of the 8 open reading frames (ORFs) of **HPV6a**, only the imputed amino acid sequence of the major capsid **protein L1** was identical to the corresponding **HPV6b** sequence; all other **HPV6a** ORFs showed amino acid changes compared to the **HPV6b** ORFs. The **HPV6a** L1 or the L1 + L2 ORFs were expressed in the yeast Saccharomyces cerevisiae. Self-assembly of the L1 capsid protein into virus-like particles (VLPs) was demonstrated both in the L1 as well as L1 + L2 coexpressing yeast strains. Copurifn. of the L1 and L2 proteins showed complex formation of the L1 and L2 proteins in the yeast-derived

VLPs of coexpressing strains.

IT **168116-30-1 168116-31-2**
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(amino acid sequence; sequence detn. of human **papillomavirus** type 6a and assembly of virus-like particles in Saccharomyces cerevisiae)

IT **168116-24-3 168116-25-4 168116-26-5**
168116-27-6 168116-28-7 168116-29-8
RL: PRP (Properties)
(amino acid sequence; sequence detn. of human **papillomavirus** type 6a and assembly of virus-like particles in Saccharomyces cerevisiae)

IT **165473-82-5**, GenBank L41216
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; sequence detn. of human **papillomavirus** type 6a and assembly of virus-like particles in Saccharomyces cerevisiae)

L9 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:673496 HCAPLUS
DOCUMENT NUMBER: 121:273496
TITLE: Canine oral **papillomavirus** genomic sequence: a unique 1.5-kb intervening sequence between the E2 and L2 open reading frames
AUTHOR(S): Delius, Hajo; Van Ranst, Marc A.; Jenson, A. Bennett; zur Hausen, Harald; Sundberg, John P.
CORPORATE SOURCE: Forschungsschwerpunkt Angewandte Tumorvirologie, Deutsches Krebsforschungszentrum, Heidelberg, D-6900, Germany
SOURCE: Virology (1994), 204(1), 447-52
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The canine oral **papillomavirus** (COPV) is assocd. with oropharyngeal **papillomatosis** in dogs, coyotes, and wolves. The authors have detd. the complete nucleotide sequence of COPV, the largest of all known PV genomes (8607 bp). The genomic architecture of the COPV genome is similar to that of other PVs except for a unique and large noncoding region of 1.5 kb between the end of the early region (E2) and the beginning of the late region (L2) and a small (345 bp) upstream regulatory region between the end of L1 and the beginning of E6. Although COPV displays a primarily mucosal tropism, the COPV nucleotide sequence showed the highest overall similarity to cutaneous **papillomaviruses** such as **HPV**-1, **HPV**-63, CRPV (cottontail rabbit PV), FdPV (Felis domesticus PV), and MnPV (Mastomys natalensis PV).

IT **158888-99-4**, Protein E6 (canine oral **papillomavirus**)
158889-00-0, Protein E7 (canine oral **papillomavirus**)
158889-01-1, Protein E1 (canine oral **papillomavirus**)
158889-02-2, Protein E2 (canine oral **papillomavirus**)
158889-03-3 158889-05-5
RL: PRP (Properties)
(amino acid sequence; genomic sequence and a unique 1.5-kb intervening sequence between the E2 and L2 open reading frames of canine oral

papillomavirus)

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=> d stat que

L1          164 SEA FILE=REGISTRY HPV?
L2          872 SEA FILE=REGISTRY PROTEIN E?/CN
L3           74 SEA FILE=REGISTRY "PROTEIN L1"?/CN
L4       172330 SEA FILE=HCAPLUS L1 OR HPV? OR PAPILLOMA?
L5         1659 SEA FILE=HCAPLUS PROTEIN(W)E OR L2
L6          910 SEA FILE=HCAPLUS "PROTEIN L1"? OR L3
L8           19 SEA FILE=HCAPLUS L5 AND L6
L9            5 SEA FILE=HCAPLUS L4 AND L8
L10        2069 SEA FILE=HCAPLUS PROTEIN(W)E#
L11        2607 SEA FILE=HCAPLUS L2 OR L10
L12         885 SEA FILE=HCAPLUS PROTEIN(W)L1?
L13         910 SEA FILE=HCAPLUS L6 OR L12
L14          34 SEA FILE=HCAPLUS L11 AND L13
L15          19 SEA FILE=HCAPLUS L14 AND L4
L16          14 SEA FILE=HCAPLUS L15 NOT L9


=> d ibib abs hitrn l16 1-14


L16  ANSWER 1 OF 14  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         1998:102997  HCAPLUS
DOCUMENT NUMBER:          128:153148
TITLE:                    Method for activating the immune system against cells
                          associated with papilloma viruses or their
                          sequences
INVENTOR(S):              Kleinschmidt, Juergen; Jochmus, Ingrid; Gissmann,
                          Lutz; Mueller, Martin
PATENT ASSIGNEE(S):       Deutsches Krebsforschungszentrum Stiftung des
                          Oeffentlichen Rechts, Germany
SOURCE:                   Ger. Offen., 4 pp.
                          CODEN: GWXXBX
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     DE 19631357        A1   19980205       DE 1996-19631357 19960802
     WO 9805790         A1   19980212       WO 1997-DE1629   19970730
         W:  JP, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     EP 917586          A1   19990526       EP 1997-935500   19970730
         R:  AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE
PRIORITY APPLN. INFO.:                      DE 1996-19631357 19960802
                                            WO 1997-DE1629   19970730
AB   A vaccine against cells infected with human papillomavirus (
     HPV) comprises a vector contg. a nucleic acid which encodes a
     fusion polypeptide, where the fusion polypeptide consists of a structural
     papillomavirus (poly)peptide and a nontransforming (poly)peptide
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encoded by an early **papillomavirus** gene. Thus, the open reading frame (ORF) encoding C-terminally truncated major capsid **protein L1** of **HPV** 16 was amplified by PCR, inserted into vector pUC19, and ligated to an ORF fragment encoding the 1st 50 amino acids of **protein E6** of **HPV** 16; the deletion from E6 destroys the transforming properties of the transcript. The L1-E6 fusion gene was excised and inserted into adeno-assocd. virus vector pUF2.

L16 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:18407 HCAPLUS
DOCUMENT NUMBER: 128:125687
TITLE: The **papillomavirus** minor capsid protein, L2, induces localization of the major capsid **protein, L1**, and the viral transcription/replication **protein, E2**, to PML oncogenic domains
AUTHOR(S): Day, Patricia M.; Roden, Richard B. S.; Lowy, Douglas R.; Schiller, John T.
CORPORATE SOURCE: Laboratory of Cellular Oncology, Division of Basic Sciences, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: J. Virol. (1998), 72(1), 142-150
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have used immunofluorescent staining and confocal microscopy to examine the subcellular localization of structural and nonstructural bovine **papillomavirus** (BPV) proteins in cultured cells that produce infectious virions. When expressed sep., L1, the major capsid protein, showed a diffuse nuclear distribution while L2, the minor capsid protein, was found to localize to punctate nuclear regions identified as promonocytic leukemia protein (PML) oncogenic domains (PODs). Coexpression of L1 and L2 induced a relocation of L1 into the PODs, leading to the colocalization of L1 and L2. The effect of L2 expression on the distribution of the nonstructural viral proteins E1 and E2, which are required for maintenance of the genome and viral DNA synthesis, was also examd. The localization of the E1 protein was unaffected by L2 expression. However, the pattern of anti-E2 staining was dramatically altered in L2-expressing cells. Similar to L1, E2 was shifted from a dispersed nuclear locality into the PODs and colocalized with L2. The recruitment of full-length E2 by L2 occurred in the absence of other viral components. L2 was shown previously to be essential for the generation of infectious BPV. Our present results provide evidence for a role for L2 in the organization of virion components by recruiting them to a distinct nuclear domain. This L2-dependent colocalization probably serves as a mechanism to promote the assembly of **papillomaviruses** either by increasing the local concn. of virion constituents or by providing the phys. architecture necessary for efficient packaging and assembly. The data also suggest a role for a nonstructural viral **protein, E2**, in virion assembly, specifically the recruitment of the viral genome to the sites of assembly, through its high-affinity interaction with specific sequences in the viral DNA.

L16 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:640855 HCAPLUS

DOCUMENT NUMBER: 125:294153
TITLE: A comparison of early (E7) and late (L1) primer-mediated amplification of **papillomaviral** DNA in cervical neoplasia
AUTHOR(S): Tate, James E.; Yang, Yuh-Cheng; Shen, Jian; McLachlin, Catherine M.; Sheets, Ellen E.; Crum, Christopher P.
CORPORATE SOURCE: Dep. Pathology, Brigham's and Women's Hospital, Boston, MA, USA
SOURCE: Mol. Cell. Probes (1996), 10(5), 347-351
CODEN: MCPRE6; ISSN: 0890-8508
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies have demonstrated that in 50-90% of cervical carcinomas, human **papillomavirus** (**HPV**) DNA sequences are covalently bound (integrated) to the chromosomal DNA. All evidence shows that when integration takes place disruption of the viral genome occurs downstream to the E7 open reading frame, which is invariably retained in functional form. Theor., this phenomenon could result in loss of **HPV** sequences (L1) not crit. to the presumed tumorigenic functions and if so, could influence primer selection for **HPV** DNA detection in these tumors. A series of cervical carcinomas (CA, n = 133), adenocarcinomas in situ (ACIS, n = 28) and high grade squamous intraepithelial lesions (HSIL, n = 30) were analyzed for **HPV** nucleic acids using primers designed to amplify the E7 and L1 regions. Primer sizes and sensitivities were adjusted to produce equiv. amplification efficiency. Of 191 cases studied, 134 (70%) scored pos. for **HPV16** or 18 with either the E7 or L1 primer set. Of these, 116 (87%) were pos. with both primer pairs. There were no significant differences in proportions of **HPV** 16/18 positives or lesion types scoring pos. exclusively with the E7 vs the L1 primer sets. However, **HPV18** assocd., E7 pos. carcinomas were slightly less likely than **HPV16** assocd. carcinomas to be L1 pos. (P = 0.07). Although a high proportion of **HPV16** and particularly **HPV18** pos. carcinomas have been assocd. with exclusively integrated **HPV** DNA, there is little evidence that this influences detection sensitivity with E7 vs L1 primers. The combination of E7 and L1 primers provided the max. sensitivity in this study, with 18 of 134 cases scoring pos. with only one primer set.

L16 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:293730 HCAPLUS
DOCUMENT NUMBER: 120:293730
TITLE: Colocalization of human **papillomavirus** type 11 E1 E4 and L1 proteins in human foreskin implants grown in athymic mice
AUTHOR(S): Brown, Darron R.; Fan, Li; Jones, Julie; Bryan, Janine
CORPORATE SOURCE: Dep. Med., Richard L. Roudebush Veterans Adm. Med. Cent., Indianapolis, IN, 46202, USA
SOURCE: Virology (1994), 201(1), 46-54
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The most abundant viral mRNA species in tissues infected with **HPV** 11 consists of two exons, joining a short segment of open reading frame (ORF) E1 to ORF E4, potentially encoding an E1 E4 protein of 10 kDa. E4 gene products have previously been identified by immunohistochem. in human

tissues infected with **HPV** 1 and **HPV** 16, and in **HPV** 11-infected rat cultures. The E1 E4 mRNA is produced in abundance in **HPV** 11-infected human foreskin implants grown in athymic mice. In contrast, the L1 mRNA is present at low levels and appears late in the course of infection. To characterize the relationship of these proteins, polyclonal rabbit antisera were produced against bacterially expressed **HPV** 11 trpE/E1 E4 and trpE/L1 fusion proteins and tested in an immunohistochem. assay of paraffin-embedded sections of **HPV** 11-infected human foreskin tissue fixed with 10% buffered formalin phosphate or zinc formalin. In sections fixed with either fixative, the anti-L1 serum stained nuclei of cells in the upper spinous and granular layers. In contrast, the anti-E1 E4 serum stained the cell membrane and, to a lesser degree, the cytoplasm of cells in the upper spinous and granular layers of tissue fixed with zinc formalin, but not 10% buffered formalin phosphate. In sections treated with both the E1 E4 and Li antisera, cell membrane staining occurred in the same cells that exhibited nuclear staining. The **HPV** 11 E1 E4 protein appears to be a cell membrane-assocd. protein. Expression of the **HPV** 11 E1 E4 and L1 proteins may be influenced by similar factors in differentiating cells.

L16 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:6610 HCAPLUS
DOCUMENT NUMBER: 120:6610
TITLE: Relation between skin cancer, humoral responses to human **papillomaviruses**, and HLA class II molecules in renal transplant recipients
AUTHOR(S): Bavinck, Jan N. Bouwes; Gissmann, Lutz; Claas, Frans H. J.; Van Der Woude, Fokko J.; Persijn, Guido G.; Ter Schegget, Jan; Vermeer, Bert J.; Jochmus, Ingrid; Mueller, Martin; et al.
CORPORATE SOURCE: Dep. Dermatol., Univ. Hosp., Leiden, 2333 AA, Neth.
SOURCE: J. Immunol. (1993), 151(3), 1579-86
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human **papillomaviruses** (**HPV**), esp. the epidermodysplasia verruciformis (EV)-assocd. **HPV** 5, 8, 14, 17, 20, and 47, are thought to play a role in the pathogenesis of some skin cancers in recipients of renal allografts. MHC class I and class II genes are involved in the cellular immune response to viral and tumor antigen (Ag). Little is known about humoral responses to **HPV** in recipients with and without skin cancer. The authors investigated the prevalence of antibodies to the early (E) **protein E7** and the major capsid late (L) **protein L1** and **HPV** 8. In addn., the authors studied the assocn. of HLA class II mols. with these antibody responses. The E7 and L1 open reading frames of **HPV** 8 were bacterially expressed as .beta.-galactosidase fusion proteins, which were purified by preparative gel electrophoresis. Serum samples from 36 renal transplant recipients with and 91 recipients without skin cancer were screened for the presence of IgG and IgM antibodies to **HPV** 8 E7 and L1, by Western blot anal. The detection of anti-**HPV** 8 L1 antibodies represents the immune response to **HPV** 8 and possibly other EV-assocd. **HPV**, because cross-reactivity between the representatives of this **HPV** subgenus can occur. Recipients who had IgM antibodies but no IgG antibodies to L1 of

HPV 8 (patients with no apparent class switch from IgM to IgG) had skin cancer in 50% of cases, whereas recipients who produced IgG antibodies had skin cancer in only 18% of cases. The estd. relative risk of skin cancer in recipients with no class switch, compared with the risk in those with a good humoral response, was 4.5. The authors found no assocn. between the antibody prodn. in response to L1 of **HPV** 8 and HLA-DR7 was obsd. Renal transplant recipients who have no apparent class switch from IgM to IgG prodn. in response to Ag encoded by L1 of **HPV** 8 or possibly other EV-assocd. **HPV** are at an increased risk of skin cancer. The assocn. with HLA-DR7 indicates a genetic control of skin cancer development or regression, involving genes in the class II region of the MHC.

L16 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:606035 HCAPLUS
DOCUMENT NUMBER: 117:206035
TITLE: Genetic heterogeneity among human **papillomaviruses** (**HPV**) associated with epidermodysplasia verruciformis: evidence for multiple allelic forms of **HPV5** and **HPV8** E6 genes
AUTHOR(S): Deau, Marie Christine; Favre, Michel; Orth, Gerard
CORPORATE SOURCE: Unite Papillomavirus, Inst. Pasteur, Paris, 75725, Fr.
SOURCE: Virology (1991), 184(2), 492-503
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To gain insight into modifications of human **papillomavirus** (**HPV**) genomes which could play a role in tumor progression in epidermodysplasia verruciformis (EV), the authors studied three EV patients infected by **HPV5** and one by **HPV8**, with cancers contg. mostly or only episomal viral genomes with a deletion. The mutants were compared with the full-length genomes present in the benign lesions of each patient. Deletions affected the L1 and/or L2 open reading frames (ORFs), and extended in the 5' end of the long control region in two cancers. The isolates studied showed a polymorphism of restriction endonuclease cleavage sites and variations in the nucleotide sequence of the E6 ORF and the regions flanking the deletions. However, except for one patient infected by two distinct **HPV5** variants, no difference was obsd. in the nucleotide sequence of isolates cloned from the benign lesions and the cancer of the same patient. This may suggest that point mutations are not involved in tumor progression. Comparison of nucleotide sequence data revealed an unexpectedly high no. of nucleotide substitutions among the four **HPV5** variants and the **HPV8** variant, as compared with **HPV5** and **HPV8** published sequences. Changes involved 49 of the 457 nucleotides of **HPV5** E6 ORF and 14 of the 465 nucleotides of **HPV8** E6 ORF. This corresponds to amino acid substitutions affecting 17 of the 157 amino acids of **HPV5** E6 proteins and 7 of the 155 amino acids of **HPV8** E6 proteins. Half of the substitutions represent nonconservative changes. The variants showing the highest degree of sequence variation were detected in addnl. EV patients by PCR. This points to the existence of a set of **HPV5** and **HPV8** stable variants, encoding for multiple allelic forms of the transforming E6 gene.

L16 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:525633 HCAPLUS
DOCUMENT NUMBER: 117:125633
TITLE: Characterization of a novel human **papillomavirus** DNA in the cervical carcinoma cell line ME180
AUTHOR(S): Reuter, Stella; Delius, Hajo; Kahn, Tomas; Hofmann, Birgit; Zur Hausen, Harald; Schwarz, Elisabeth
CORPORATE SOURCE: Projektgruppe Angew. Tumorvirol., Dtsch. Krebsforschungszent., Heidelberg, 6900, Germany
SOURCE: J. Virol. (1991), 65(10), 5564-8
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human cervical carcinoma cell line ME180 was examd. for human **papillomavirus** (**HPV**) DNA and RNA. The integrated DNA of a presumably new **HPV** type showing a relationship closer to **HPV39** than to **HPV18** was cloned and sequenced. **HPV** sequences from the E6-E7-E1 region are expressed as poly(A)+ RNAs.

L16 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:507225 HCAPLUS
DOCUMENT NUMBER: 115:107225
TITLE: Characterization of the complete RhPV 1 genomic sequence and an integration locus from a metastatic tumor
AUTHOR(S): Ostrow, Ronald S.; LaBresh, Kurt V.; Faras, Anthony J.
CORPORATE SOURCE: Med. Sch., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Virology (1991), 181(1), 424-9
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complete nucleotide sequence of the rhesus **papillomavirus** type 1 (RhPV 1) genome was detd. The genome is 8026 nucleotide in length and has a genomic organization similar to that of other characterized **papilloma** viruses. Sequence comparison of RhPV 1 to other **papillomaviruses** found similarities closest to **HPV** 16, a sexually transmitted human virus with a high oncogenic potential. Slight differences in the glucocorticoid-responsive elements may explain disparate reliance upon added dexamethasone for transformation in vitro these 2 **papillomaviruses**. In addn., a previously described DNA clone consisting of contiguous RhPV 1 and cellular sequences was partially sequenced. The disruption of the RhPV 1 genome due to integration occurred within the L1 open reading frame RhPV 1, and no significant similarities were obsd. between the adjacent cellular sequences and information in various data banks.

L16 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:486278 HCAPLUS
DOCUMENT NUMBER: 115:86278
TITLE: A comparative sequence analysis of two human **papillomavirus** (**HPV**) types 2a and 57
AUTHOR(S): Hirsch-Behnam, Anja; Delius, Hajo; De Villiers, Ethel Michele

CORPORATE SOURCE: Inst. Angew. Tumorvirol., Dtsch. Krebsforschungszent., Heidelberg, 6900, Fed. Rep. Ger.
SOURCE: Virus Res. (1990), 18(1), 81-97
CODEN: VIREDF; ISSN: 0168-1702
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The complete DNA sequences of **HPV** 2a and **HPV** 57 were detd. The **HPV** 2a genome consists of 7860 base pairs and the **HPV** 57 genome contains 7861 base pairs. On the nucleotide level an 83% homol. between the 2 sequences could be ascertained. Compared to other **HPVs** they have a high G/C-content (**HPV** 2a: 48.8%, **HPV** 57: 50.1%). The genomic organization of both viruses complies with that of other sequenced **HPVs**. Significant sequence divergence between the **HPV** 2a and **HPV** 57 genomes was found in the long control region (LCR), as well as in the early-late-region (ELR). The latter varies in size between the cutaneous (72-103 nucleotides) and the mucosal **HPVs** (252-584 nucleotides). According to the sizes of the ELRs of **HPV** 2a (377 nucleotides) and **HPV** 57 (478 nucleotides), as well as DNA sequence comparisons, these 2 viruses could be grouped with the so-called mucosal **HPVs**. In a search for possible tissue-specific elements, a common amino acid motif, Thr-Thr/Asp-Pro-Ala-Ile/Val-Ile/Leu was found in the L2 of all mucosal **HPVs**, as well as in **HPV** 2a and 57. The L2 of the cutaneous types contains the motif Val-Ser/Thr-Arg-Thr-Gln-Tyr.

L16 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:173126 HCAPLUS
DOCUMENT NUMBER: 112:173126
TITLE: Nucleotide sequence of human **papillomavirus** type 31: a cervical neoplasia-associated virus
AUTHOR(S): Goldsborough, Mindy D.; DiSilvestre, Debbie; Temple, Gary F.; Lorincz, Attila T.
CORPORATE SOURCE: Div. Mol. Diagn. Res., Life Technol., Inc., Gaithersburg, MD, 20877, USA
SOURCE: Virology (1989), 171(1), 306-11
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The nucleotide sequence of human **papillomavirus** (**HPV**) 31 DNA (7912 bp) was detd. and used to deduce the genomic organization of this cervical cancer-assocd. virus. Basement on comparisons of the **HPV** 31 DNA sequence to other sequenced **HPVs**, **HPV** 31 is a typical **papillomavirus** most related to **HPV** 16 (70% identical nucleotides). The E6 and E7 open reading frames (ORF) of **HPV** 31 contain several potential DNA binding motifs (Cys-X-X-Cys), the locations of which are conserved in all **HPVs**. The E6 ORF also has the potential to code for an E6* protein. The E7 ORF of **HPV** 31 encodes a polypeptide motif which appears to distinguish **HPVs** assocd. with cervical cancer, such as types 16, 18, 31, and 33, from **HPVs** from primarily in benign lesions, such was types 6 and 11.

L16 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:588504 HCAPLUS
DOCUMENT NUMBER: 111:188504
TITLE: Characterization of rare human **papillomavirus**

type 11 mRNAs coding for regulatory and structural proteins, using the polymerase chain reaction
AUTHOR(S): Rotenberg, Mitch O.; Chow, Louise T.; Broker, Thomas R.
CORPORATE SOURCE: Sch. Med., Univ. Rochester, Rochester, NY, 14642, USA
SOURCE: Virology (1989), 172(2), 489-97
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Certain human **papillomavirus** (**HPV**) types cause warts, dysplasias, and carcinomas of the ano-genital and oral mucosa. Because of the inability to propagate **HPVs** in cultured cells, the paucity of viral mRNAs in human lesions, and the complexity of alternatively spliced transcripts derived from different promoters, it has not been possible to ascertain the exact structures of the majority of the mRNA species and the proteins encoded. The polymerase chain reaction was adapted to amplify cDNAs of rare, type 11 **HPV** mRNAs isolated from a productively infected human foreskin xenograft in an athymic mouse. The oligonucleotide primers were designed to flank each of the mRNA splice sites previously mapped by electron microscopic anal. of heteroduplexes formed between cloned **HPV**-11 DNA and viral mRNAs isolated from genital warts. The splice junctions were detd. by direct sequencing of the PCR-amplified cDNA products or after the cDNA was cloned into a plasmid vector. This provides the first direct evidence for the existence of rare mRNAs with the potential to encode regulatory proteins that have been hypothesized to exist for **HPVs**. Depending on the lengths of the upstream exons, the translation frame used and the possibility of internal reinitiation during translation, one pair of mRNAs with the same splice junction could encode the viral DNA copy no. modulating **protein E1**-M, the enhancer repression **protein E2**-C, or both. A second pair of mRNAs, also with identical splice junctions, encode the enhancer-regulating **protein E2**; the longer of the 2 could also encode, in its 5' exon, either or both the E6 and E7 proteins. Finally, the doubly spliced late message for the major virion capsid **protein L1** also contains the entire coding region for the early E1-E4 protein in the first 2 exons, with the initiation codon for the L1 protein located precisely at the splice acceptor of the third exon. The potential of this late mRNA to encode both the E1-E4 protein and the capsid protein could contribute to the preponderance of the E4 protein in the lesion.

L16 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:16940 HCAPLUS
DOCUMENT NUMBER: 108:16940
TITLE: The nucleotide sequence and genome organization of bovine **papillomavirus** type 4
AUTHOR(S): Patel, Kamalesh R.; Smith, Kenneth T.; Campo, M. Saveria
CORPORATE SOURCE: Beatson Inst. Cancer Res., Glasgow, G61 1BD, UK
SOURCE: J. Gen. Virol. (1987), 68(8), 2117-28
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The nucleotide sequence of bovine **papillomavirus** type 4 (BPV-4) was detd. The viral genome is 7261 base pairs long. Several overlapping open reading frames (ORFs) were identified both on the basis of amino acid

comparison with other **papillomaviruses** and on their transcriptional pattern. Eight early ORFs (E1 to 8), coding for DNA replication and cell transformation functions and 3 late ORFs (L1 to 3), coding for structural proteins, were recognized. Like the E5 ORF of human **papillomavirus** type 6 the E5 ORF of BPV-4 is discontinuous. Unlike other **papillomaviruses**, the non-coding region upstream of the early ORFs (ncr-1) is short (385 base pairs), but there is another non-coding region (ncr-2) of nearly 500 base pairs between the L2 and L1 ORFs. Most of the putative regulatory sites are located in the ncr-1, although potential controlling elements are also found in other parts of the genome. Polyadenylation sites are present at the 3' end of both the early and the late transcription units. Comparison between the polypeptides of BPV-4 and other **papillomaviruses** showed that BPV-4 is evolutionarily closer to the epitheliotropic human and rabbit viruses than to BPV-1.

L16 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:1111 HCAPLUS
DOCUMENT NUMBER: 106:1111
TITLE: Genome organization and nucleotide sequence of human **papillomavirus** type 33, which is associated with cervical cancer
AUTHOR(S): Cole, Stewart T.; Streeck, Rolf E.
CORPORATE SOURCE: Group. Genie Genet., Inst. Pasteur, Paris, 75724, Fr.
SOURCE: J. Virol. (1986), 58(3), 991-5
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 7909-nucleotide sequence of human pappillomavirus type 33, which is assocd. with cervical cancer, was detd. and used to deduce the corresponding genome arrangement. Extensive sequence homologies and other genetic features are shared with the related oncogenic virus, human pappillomavirus type 16, esp. in the major reading frames. A surprising difference was found in the noncoding region of human **papillomavirus** type 33 as, unlike all other sequenced **papillomaviruses**, it contains a perfect 78-base-pair tandem repeat.

L16 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:554979 HCAPLUS
DOCUMENT NUMBER: 103:154979
TITLE: Human **papillomavirus** type 16 DNA sequence
AUTHOR(S): Seedorf, Klaus; Kraemmer, Guenter; Duerst, Matthias; Suhai, Sandor; Rowekamp, Walter G.
CORPORATE SOURCE: Inst. Cell Tumor Biol., Ger. Cancer Res. Cent., Heidelberg, 6900, Fed. Rep. Ger.
SOURCE: Virology (1985), 145(1), 181-5
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complete nucleotide sequence of human **papillomavirus** 16 (**HPV16**) DNA (7904 base pairs) cloned from an invasive cervical carcinoma was detd. Homol. comparisons allowed the alignment of major open reading frames with the other published **papilloma** virus DNA sequences. The general organization of the open reading frames is similar to that of the other 4 **papillomaviruses** (PBV1, **HPV1a**,

HPV6b, CRPV) already sequenced. The sequence reveals an interruption of the reading frame for a suspected E1 protein.

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L1          164 SEA FILE=REGISTRY HPV?
L2          872 SEA FILE=REGISTRY PROTEIN E?/CN
L3           74 SEA FILE=REGISTRY "PROTEIN L1"?/CN
L4       172330 SEA FILE=HCAPLUS L1 OR HPV? OR PAPILLOMA?
L5         1659 SEA FILE=HCAPLUS PROTEIN(W)E OR L2
L6          910 SEA FILE=HCAPLUS "PROTEIN L1"? OR L3
L8           19 SEA FILE=HCAPLUS L5 AND L6
L9            5 SEA FILE=HCAPLUS L4 AND L8
L10        2069 SEA FILE=HCAPLUS PROTEIN(W)E#
L11        2607 SEA FILE=HCAPLUS L2 OR L10
L12         885 SEA FILE=HCAPLUS PROTEIN(W)L1?
L13         910 SEA FILE=HCAPLUS L6 OR L12
L14          34 SEA FILE=HCAPLUS L11 AND L13
L15          19 SEA FILE=HCAPLUS L14 AND L4
L16          14 SEA FILE=HCAPLUS L15 NOT L9
L17        1700 SEA FILE=HCAPLUS L13 OR PROTEIN(2A)L1?
L18       16583 SEA FILE=HCAPLUS L11 OR PROTEIN(2A)E#
L19          65 SEA FILE=HCAPLUS L17 AND L18 AND L4
L20          46 SEA FILE=HCAPLUS L19 NOT (L9 OR L16)


=> d ibib abs hitrn l20 1-46


L20  ANSWER 1 OF 46  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:865093  HCAPLUS
DOCUMENT NUMBER:          134:16537
TITLE:                    Cytotoxic T-cell epitopes of the
                        Papillomavirus L1-Protein
                          and their use in diagnostics and therapy
INVENTOR(S):              Schaefer, Klaus; Faath, Stefan; Jochmus, Ingrid;
                          Nieland, John; Osen, Wolfram
PATENT ASSIGNEE(S):       Medigene A.-G., Germany; Deutsches
                          Krebsforschungszentrum (DKFZ)
SOURCE:                   Ger. Offen., 26 pp.
                          CODEN: GWXXBX
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     DE 19925235        A1   20001207       DE 1999-19925235  19990601
     WO 2000073464      A1   20001207       WO 2000-EP5005    20000531
         W:  AU, CA, JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
PRIORITY APPLN. INFO.:                      DE 1999-19925235  19990601
AB   The available invention concerns Papillomavirus T-cell epitopes
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with an amino acid sequence AQIFNKPYW, AGVDNRECI, and/or a functionally active variant thereof, as well as their use in diagnostics and therapy.
REFERENCE COUNT: 3
REFERENCE(S): (1) Anon; EP 0375555 A1 HCAPLUS
(2) Anon; EP 0451550 A2 HCAPLUS
(3) Anon; WO 9302184 HCAPLUS

L20 ANSWER 2 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:865090 HCAPLUS
DOCUMENT NUMBER: 134:16536
TITLE: Cytotoxic T-cell epitopes of the **Papillomavirus** L1 proteins and their use in diagnossis and therapy
INVENTOR(S): Nieland, John; Jochmus, Ingrid
PATENT ASSIGNEE(S): Medigene A.-G., Germany
SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19925199	A1	20001207	DE 1999-19925199	19990601
WO 2000073335	A1	20001207	WO 2000-EP5006	20000531

W: AU, CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: DE 1999-19925199 19990601
AB The available invention concerns **Papillomavirus** T-cell epitopes with the amino acid sequence ILVPKVSGL, RLVWACVGV, HLFNRAGTV, YLRREQMFV, TLQANKSEV, ILEDWNFGL, SLWLPSEATVYL, NLASSNYFPT, TLTADVMTYI, YLPPVPVSKV, YDLQFIFQL, ICWGNQLFV, and/or a functionally active variant thereof, as well as their use in diagnosis and therapy.
REFERENCE COUNT: 3
REFERENCE(S): (1) Anon; EP 0375555 A1 HCAPLUS
(2) Anon; EP 0451550 A2 HCAPLUS
(3) Anon; WO 9302184 HCAPLUS

L20 ANSWER 3 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:524010 HCAPLUS
TITLE: Construction and expression of an attenuated recombinant adenovirus of human **papilloma** -virus type 16 L1-E7
AUTHOR(S): Bian, Jifeng; Yu, Xiuping; Qi, Mei; Wang, Yun; Yang, Haining; Hu, Haiyan; Geng, Zhao; Zhao, Weiming; Zhou, Yabin; Jia, Jihui
CORPORATE SOURCE: Laboratory of Molecular Biology and Dept. of Microbiology, Shandong Medical University, Jinan, 250012, Peop. Rep. China
SOURCE: Shandong Yike Daxue Xuebao (2000), 38(2), 113-116, 119
CODEN: SYXBEE; ISSN: 1000-0496
PUBLISHER: Shandong Yike Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB An attenuated recombinant adenovirus vaccine against **HPV16** infection and human cervical cancer was constructed and developed. The plasmid pUC19L1-E7 contained the major capsid **protein L1** ORF and E7 ORF was constructed using polymerase chain reaction. The L1-E7 DNA fragment was digested with HindIII and SmaI and inserted into pBluescript, named pBSL1-E7, and then the L1-E7 DNA fragment was cut with HindIII and XbaI and inserted into adenovirus shuttle plasmid pCA14, and co-transfected 293 cells with the adenovirus pBHC10 plasmid, the recombinant adenovirus of **HPV16** was harvested. The expression level of the chimeric virus-like particle was detected using ELISA, immunoassay and the electron microscopy. The fusion **L1-E7 protein** was expressed at the high level (10% of total cellular protein, TCR) and could self assembled into the chimeric virus-like particle (cVLP), which was morphol. indistinguishable from the native virus and displayed the conformational epitopes. These data indicated that the recombinant adenovirus of human **papilloma** virus type 16 L1-E7 was constructed and the **L1-E7** fusion **protein** could be expressed at high level, and could be self assemble into the chimeric virus-like particles in human cells. The recombinant pUC19L1 plasmid was an ideal vector for constructing other chimeric vaccine carried the epitopes derived from virus and tumor antigen.

L20 ANSWER 4 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:513608 HCAPLUS
DOCUMENT NUMBER: 133:265379
TITLE: **Papillomavirus** Virus-like Particles for the Delivery of Multiple Cytotoxic T Cell Epitopes
AUTHOR(S): Liu, Wen Jun; Liu, Xiao Song; Zhao, Kong Nan; Leggatt, Graham R.; Frazer, Ian H.
CORPORATE SOURCE: Center for Immunology and Cancer Research, Princess Alexandra Hospital, Woolloogabba, 4102, Australia
SOURCE: Virology (2000), 273(2), 374-382
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chimeric **papillomavirus** (PV) virus-like particles (VLPs) based on the bovine **papillomavirus** type 1 (BPV-1) **L1 protein** were constructed by replacing the 23-carboxyl-terminal amino acids of the BPV1 major **protein L1** with an artificial "polytope" minigene, contg. known CTL epitopes of human PV16 **E7 protein**, HIV IIIB gp120 P18, Nef, and reverse transcriptase (RT) proteins, and an **HPV16** E7 linear B epitope. The CTL epitopes were restricted by 3 different MHC class I alleles (H-2b, H-2d, HLA-A*0201). The chimeric **L1 protein** assembled into VLPs when expressed in SF-9 cells by recombinant baculovirus. After immunization of mice with polytope VLPs in the absence of adjuvant, serum antibodies were detected which reacted with both polytope VLPs and wild-type BPV1L1 VLPs, in addn. to the **HPV16E7** linear B cell epitope. CTL precursors specific for the **HPV16** E7, HIV P18, and RT CTL epitopes were also detected in the spleen of immunized mice. Polytope VLPs can thus deliver multiple B and T epitopes as immunogens to the MHC class I and class II pathways, extending the utility of VLPs as self-adjuvanting immunogen delivery systems. (c) 2000 Academic Press.
REFERENCE COUNT: 44

REFERENCE(S):
(1) An, L; J Virol 1997, V71, P2292 HCAPLUS
(3) Christensen, N; J Virol 1996, V70, P960 HCAPLUS
(4) Evander, M; J Virol 1997, V71, P2449 HCAPLUS
(5) Feltkamp, M; Eur J Immunol 1993, V23, P2242 HCAPLUS
(6) Feltkamp, M; Eur J Immunol 1995, V25, P2638 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:407552 HCAPLUS
DOCUMENT NUMBER: 134:40823
TITLE: Immune responses induced by BCG recombinant for human **papillomavirus** L1 and E7 proteins
AUTHOR(S): Jabbar, Ibtissam A.; Fernando, Germain J. P.; Saunders, Nick; Aldovini, Anne; Young, Richard; Malcolm, Karen; Frazer, Ian H.
CORPORATE SOURCE: Centre for Immunology and Cancer Research, Princess Alexandra Hospital, University of Queensland, Brisbane, 4012, Australia
SOURCE: Vaccine (2000), 18(22), 2444-2453
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recombinant bacille Calmette-Guerin (BCG) based vaccine delivery systems could potentially share the safety and effectiveness of BCG. The authors therefore prepd. recombinant BCG vaccines which expressed the **L1** late **protein** of the human **papillomavirus** (**HPV**) 6b or the **E7** early **protein** of the **HPV** 16. The two recombinants were evaluated as immunogens in C57BL/6J and BALB/c mice, and compared with a conventional protein/adjuvant system using E7 or L1 mixed with Quil-A adjuvant. RBCG6bL1 and rBCG16E7 primed specific immune responses, represented by DTH, T-proliferation and antibody, and rBCG16E7 induced cytotoxic immune response to **E7 protein** . The magnitude of the obsd. responses were less than those elicited by protein/adjuvant vaccine. As recombinant BCG vaccines expressing **HPV6bL1** or **HPV16E7** persist at low levels in the immunized host, they may be beneficial to prime or retain memory responses to antigens, but are unlikely to be useful as a single component vaccine strategy.
REFERENCE COUNT: 39
REFERENCE(S):
(1) Abdelhak, S; Microbiol 1995, V141, P1585 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:151026 HCAPLUS
DOCUMENT NUMBER: 132:331811
TITLE: Synthesis of viral DNA and late capsid **protein**

L1 in parabasal spinous cell layers of naturally occurring benign warts infected with human **papillomavirus** type 1

AUTHOR(S): Egawa, Kiyofumi; Iftner, Angelika; Doorbar, John; Honda, Yumi; Iftner, Thomas

CORPORATE SOURCE: Department of Dermatology, Kumamoto University School of Medicine, Kumamoto, Japan

SOURCE: Virology (2000), 268(2), 281-293
CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human **papillomavirus** type 1 (**HPV1**)-specific transcription, viral DNA replication, and viral protein expression were investigated in naturally occurring benign tumors by in situ hybridization, 5-bromodeoxyuridine (BrdU) incorporation, and immunohistochem.; results obtained differed from other **HPV** -infected benign tumors characterized so far. Moderate amts. of transcripts with a putative coding potential for E6/E7, E1, and E2 were demonstrated from the first subrabasal cell layer throughout the stratum spinosum and granulosum. In addn. very large amts. of E4 and L1 transcripts were present in the same epithelial layers. This finding was substantiated by the demonstration of **L1** and **E4** **protein** already in the bottom-most spinous cell layer. Furthermore massive amplification of the viral DNA as measured by BrdU incorporation and different methods of in situ hybridization took place in the lowest 5 to 10 suprabasal cell layers. These findings are in contrast to the assumption that late gene expression and viral DNA synthesis are restricted to the more differentiated cell layers of the epithelium and point to differences in the regulation of the vegetative life cycle between different **papillomavirus** types. (c) 2000 Academic Press.

REFERENCE COUNT: 47

REFERENCE(S):
(1) Baker, C; EMBO J 1987, V6, P1027 HCAPLUS
(2) Barksdale, S; J Virol 1993, V67, P5605 HCAPLUS
(4) Breitburd, F; Papillomaviruses: Cancer Cells 5 1987, P115 HCAPLUS
(5) Chow, L; J Virol 1987, V61, P1913 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 46 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:718867 HCAPLUS

DOCUMENT NUMBER: 131:347519

TITLE: DNA molecules encoding human **papillomavirus** 68 E6, E7, L1 proteins, their sequences and uses

INVENTOR(S): Orth, Gerard; Beaudenon, Sylvie; Longuet, Michele

PATENT ASSIGNEE(S): Institut Pasteur, Fr.; Institut Nationale de la Sante et de la Recherche Medicale

SOURCE: U.S., 25 pp., which
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5981173	A	19991109	US 1997-815667	19970211
PRIORITY APPLN. INFO.:			US 1996-11650	19960214
			US 1996-20458	19960215

AB The invention provides human **papillomavirus** type 68 (**HPV68**) DNA mols. isolated from a low grade cervical intraepithelial neoplasia cell line encoding E6, E7, L1 and L2 proteins. The invention also provides a method for detection of **HPV68** virus in a biol. sample using the **HPV68** DNA mols. presented in the invention as probes. The invention further provides a method for recombinant prodn. of **HPV68** DNA using a cloning vector contg. the **HPV68** DNA sequences presented in the invention and transforming a host cell with said vector. The DNA sequences of **HPV68** genes encoding E6, E7, and L1 proteins are provided. The invention also provided the DNA sequences of human **papillomavirus** type 70 (**HPV70**) E6, E7, **L1** and L2 **protein** genes, and compared the sequences of **HPV68** and **HPV70** to human **papillomavirus** type 39 (**HPV39**) and ME180-**HPV** (cervical carcinoma-derived ME 180 cell line). The invention showed that **HPV68** and **HPV70** were detected in genital intraepithelial neoplasia from three patients and one patient, resp. Comparison with sequence data in the literature indicates that the subgenomic ME180-**HPV** DNA fragment, cloned from a carcinoma cell line, corresponds to a **HPV68** subtype and that several **HPV** DNA fragments amplified by PCR from genital neoplasia represent worldwide distributed variants of **HPV68** and **HPV70**.

IT **173712-94-2**, DNA (human **papillomavirus** 68 gene L1 plus flanks)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(DNA mols. encoding human **papillomavirus** 68 E6, E7, L1 proteins, their sequences and uses)

IT **175702-95-1**, GenBank U22461
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; DNA mols. encoding human **papillomavirus** 68 E6, E7, L1 proteins, and comparison to human **papillomavirus** 70 sequences)

IT **173712-93-1**, GenBank X67160
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; DNA mols. encoding human **papillomavirus** 68 E6, E7, L1 proteins, their sequences and uses)

REFERENCE COUNT: 3
REFERENCE(S):
(1) Longuet; Journal of Clinical Microbiology 1996, V34(3), P738 HCAPLUS
(2) Reuter; Journal of Virology 1991, V65(10), P5564 HCAPLUS
(3) Volpers; Virology 1991, V181, P419 HCAPLUS

L20 ANSWER 8 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:640995 HCAPLUS
DOCUMENT NUMBER: 131:270952

TITLE: **Papillomavirus** antigen preparation and use in the production of immune responses
INVENTOR(S): Stanley, Margaret Anne; Zhang, Wei
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950424	A2	19991007	WO 1999-GB978	19990329
WO 9950424	A3	19991202		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9931594	A1	19991018	AU 1999-31594	19990329
EP 1066391	A2	20010110	EP 1999-913478	19990329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-6666 19980327
WO 1999-GB978 19990329

AB This invention relates to antigen prepn. comprising modified virus-like particles (VLPs) of papovaviruses, e.g. of human **papillomaviruses** (**HPV**). VLPs can comprise fusion proteins having sequence from **L1 protein** of **HPV** 16 or 18, in which the N-terminal of the sequence derived from the **L1 protein** is fused to a further **HPV protein** such as **E1** or E2, E6 or E7. The VLPs can contain a full sequence of an **L1 protein**, or an **L1** sequence with an N-terminal deletion, or an L1 sequence with an amino acid substitution mutation, and optionally a C-terminal L1 sequence deletion. The invention also relates to the prodn. and purifn. of such antigen prepns., and to corresponding recombinant-nucleic acid constructs e.g. expression cassettes, plasmids, recombinant cells and recombinant viruses applicable to such prodn. The invention further relates to the use of such antigenic prepns. in the prodn. of immune responses, and to vaccines based on such prepns.

L20 ANSWER 9 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:626063 HCAPLUS
DOCUMENT NUMBER: 131:241978
TITLE: **Papillomavirus L1 protein** - and **E protein**-derived fusion protein medicament for preventing or treating **papilloma** virus-specific tumors
INVENTOR(S): Burger, Alexander; Hallek, Michael
PATENT ASSIGNEE(S): Medigene Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948518	A2	19990930	WO 1999-EP1996	19990324
WO 9948518	A3	19991202		
W: AU, CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19812941	A1	19991007	DE 1998-19812941	19980324
AU 9935214	A1	19991018	AU 1999-35214	19990324
EP 1064014	A2	20010103	EP 1999-916884	19990324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: DE 1998-19812941 19980324
WO 1999-EP1996 19990324

AB A medicament is provided for preventing or treating human **papilloma** virus (**HPV**)-specific tumors which contains at least one fusion protein and optional suitable additives and/or auxiliary agents. The fusion protein is comprised of at least one **L1 protein** of one or more **papilloma** viruses and at least one **E-protein** of one or more **papilloma** viruses, whereby the fusion protein does not contain any **papilloma** virus nonspecific epitopes.

L20 ANSWER 10 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:244768 HCAPLUS
DOCUMENT NUMBER: 130:280851
TITLE: Vaccines containing L1 capsomere fusion proteins for prevention and treatment of human **papillomavirus** infection
INVENTOR(S): Gissmann, Lutz; Muller, Martin
PATENT ASSIGNEE(S): Loyola University of Chicago, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9918220	A1	19990415	WO 1998-US20965	19981006
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9896846	A1	19990427	AU 1998-96846	19981006

EP 1021547 A1 20000726 EP 1998-950930 19981006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
NO 2000001768 A 20000602 NO 2000-1768 20000406
PRIORITY APPLN. INFO.: US 1997-944368 19971006
WO 1998-US20965 19981006

AB The invention provides vaccine formulations comprising chimeric human **papilloma** virus capsomeres and methods for prodn. and purifn. of said capsomeres. According to the present invention, vaccine formulations comprise either: (i) a first protein that is an intact viral protein expressed as a fusion protein comprised in part of amino acid residues from a second protein; (ii) a truncated viral protein; (iii) a truncated viral protein expressed as a fusion protein comprised in part of amino acid residues from a second protein, or (iv) some combination of the three types of proteins. The invention also provides therapeutic methods for treating patients infected with **HPV** as well as prophylactic methods for preventing **HPV** infection in a susceptible individual..

REFERENCE COUNT: 6
REFERENCE(S): (1) Gissmann, L; DE 4435907 A 1996 HCAPLUS
(2) LI, M; JOURNAL OF VIROLOGY 1997, V71(4), P2988 HCAPLUS
(3) Muller, M; VIROLOGY 1997, V234(1), P93 HCAPLUS
(4) Paintsil, J; VIROLOGY 1996, V223(1), P238 HCAPLUS
(6) Us Department Of Health; WO 9611274 A 1996 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:13459 HCAPLUS
DOCUMENT NUMBER: 130:250311
TITLE: Human **papillomavirus**-5b DNA integrated in a metastatic tumor: cloning, nucleotide sequence and genomic organization
AUTHOR(S): Yabe, Yoshiro; Sakai, Akiko; Hitsumoto, Takako; Hanafusa, Hiroko; Jitsumori, Yoshimi; Ogura, Hajime
CORPORATE SOURCE: Institute Cellular Molecular Biology, Okayama University Medical School, Okayama, Japan
SOURCE: Int. J. Cancer (1999), 80(2), 334-335
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human **papillomavirus** type 5b DNA has been sequenced from a primary carcinoma cell of a patient with epidermodysplasia verruciformis. A BamHI fragment from the cellular DNA contg. integrated human **papillomavirus** 5b of the same patient was sequenced. The sequence was contained the C-terminal fragment of the **L1 protein**, **E6** and **E7** proteins, and the N-terminal fragment of the **E1 protein**. The E6, E7, and noncoding region between L1 and E6 were wholy preserved and free of point mutations or modifications. Another integrated viral DNA segment known to occur could not be cloned. The E6, E7 and noncoding region were essential for cellular malignancy but their point mutations or modifications were not necessarily needed for the development and/or progress of malignancy.

REFERENCE COUNT: 6
REFERENCE(S): (1) Deau, M; Virology 1991, V184, P492 HCAPLUS

(2) Grassmann, K; Int J Cancer 1996, V68, P265 HCAPLUS
(3) Orth, G; Viruses in naturally occurring cancers 1980, P259 HCAPLUS
(5) Yabe, Y; Virology 1991, V183, P793 HCAPLUS
(6) zur Hausen, H; Biochim biophys Acta 1996, V1288, PF55 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:791921 HCAPLUS
DOCUMENT NUMBER: 130:149367
TITLE: Nucleotide sequence and phylogenetic classification of human **papillomavirus** type 67
AUTHOR(S): Kirii, Yasuyuki; Matsukura, Toshihiko
CORPORATE SOURCE: New Drug Discovery research Laboratory, Kanebo LTD., Tomobuchi-cho, Miyakojima-ku, Osaka, 534, Japan
SOURCE: Virus Genes (1998), 17(2), 117-121
CODEN: VIGEET; ISSN: 0920-8569
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complete nucleotide sequence of human **papillomavirus** type 67 (**HPV** 67) cloned from a vaginal intraepithelial neoplasia, has been detd. It consists of 7801 nucleotides with a GC content of 38.4% and exhibits similar genome organizations of genital **HPVs**. By phylogenetic anal. based on the full nucleotide sequences fo E6 open reading frame of 28 genital **HPVs**, **HPV** 67 was clustered with **HPV** 16, 31, 33, 34, 35, 52, and 58.
IT **220245-52-3**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; nucleotide sequence and phylogenetic classification of human **papillomavirus** type 67)
REFERENCE COUNT: 5
REFERENCE(S): (1) Chan, S; J Virol 1995, V69, P3074 HCAPLUS
(2) Kirii, Y; Virology 1991, V185, P424 HCAPLUS
(3) Lungu, O; J Virol 1991, V65, P4216 HCAPLUS
(4) Matsukura, T; Int J Cancer 1995, V61, P13 MEDLINE
(5) Sugase, M; Int J Cancer 1997, V72, P412 MEDLINE

L20 ANSWER 13 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:704767 HCAPLUS
DOCUMENT NUMBER: 130:64941
TITLE: L1-specific protection from tumor challenge elicited by **HPV16** virus-like particles
AUTHOR(S): De Bruijn, Marloes L. H.; Greenstone, Heather L.; Vermeulen, Hans; Melief, Cornelis J. M.; Lowy, Douglas R.; Schiller, John T.; Kast, W. Martin
CORPORATE SOURCE: Department of Immunohematology and Blood Bank, University Hospital Leiden, Leiden, 2300 RC, Neth.
SOURCE: Virology (1998), 250(2), 371-376
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A single injection of **HPV16** L1 virus-like particles induced

potent CD8-mediated protection from tumor challenge by C3 cells, a line derived from embryonic mouse cells transfected with the **HPV16** genome. L1 RNA, but not protein, was detected biochem. in C3 cells. These results indicate that low-level expression of **HPV16** L1 can occur in proliferating cells and serve as a tumor vaccine target. Although L1 expression is generally thought to be restricted to terminally differentiated epithelial cells, these results suggest that addnl. anal. for low-level L1 expression in proliferating cells of **HPV** -induced lesions is warranted and might help in predicting the clin. potential of **HPV** L1 virus-like particle-based vaccines. (c) 1998 Academic Press.

REFERENCE COUNT: 23

REFERENCE(S):
(1) Brown, M; Nature 1991, V353, P355 HCAPLUS
(2) Christensen, N; Virology 1996, V223, P174 HCAPLUS
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(5) Feltkamp, M; Eur J Immunol 1993, V23, P2242 HCAPLUS
(6) Feltkamp, M; Eur J Immunol 1995, V25, P2638 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 14 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:239292 HCAPLUS
DOCUMENT NUMBER: 128:279563
TITLE: Manufacture of human **papillomavirus** proteins for vaccine use in attenuated microbial expression hosts
INVENTOR(S): Haefliger, Denise Nardelli; Kraehenbuhl, Jean-Pierre
PATENT ASSIGNEE(S): Fondation Pour Le Perfectionnement Et La Recherche En Gynecologie-Obstetriqu, Switz.; Kiddle, Simon, John; Haefliger, Denise Nardelli; Kraehenbuhl, Jean-Pierre
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815631	A1	19980416	WO 1997-GB2740	19971007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9745668	A1	19980505	AU 1997-45668	19971007
EP 932683	A1	19990804	EP 1997-944023	19971007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9711881	A	20000118	BR 1997-11881	19971007
PRIORITY APPLN. INFO.:			GB 1996-21091	19961009
			WO 1997-GB2740	19971007

AB Human **papillomavirus** (**HPV**) proteins are manufd. in attenuated prokaryotic expression hosts for use as antigens in vaccines against the virus and thereby decreasing the risk of **HPV**-assocd. cancer. The proteins can be assembled into virus-like particles that can be used in vaccines. The preferred host is a PhoPc mutant of Salmonella typhimurium. Nasal immunization of mice with these particles led to strains-specific conformationally dependent and neutralizing antibodies in serum and genital secretions. The expts. also show that it is possible to assemble chimeric VLPs of an **HPV** including a fusion partner and that tumor protection can be induced.

L20 ANSWER 15 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:121999 HCAPLUS
DOCUMENT NUMBER: 128:242731
TITLE: Chimeric **papillomavirus** virus-like particles elicit antitumor immunity against the E7 oncoprotein in an **HPV16** tumor model
AUTHOR(S): Greenstone, Heather L.; Nieland, John D.; De Visser, Karin E.; De Bruijn, Marloes L. H.; Kirnbauer, Reinhard; Roden, Richard B. S.; Lowy, Douglas R.; Kast, W. Martin; Schiller, John T.
CORPORATE SOURCE: Laboratory of Cellular Oncology, National Institutes of Health, Bethesda, MD, 20892-4040, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1998), 95(4), 1800-1805
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Papillomavirus**-like particles (VLPs) are a promising prophylactic vaccine candidate to prevent human **papillomavirus** (**HPV**) infections and assocd. epithelial neoplasia. However, they are unlikely to have therapeutic effects because the virion capsid proteins are not detected in the proliferating cells of the infected epithelia or in cervical carcinomas. To increase the no. of viral antigen targets for cell-mediated immune responses in a VLP-based vaccine, we have generated stable chimeric VLPs consisting of the **L1** major capsid **protein** plus the entire E7 (11 kDa) or E2 (43 kDa) nonstructural **papillomavirus** protein fused to the L2 minor capsid protein. The chimeric VLPs are indistinguishable from the parental VLPs in their morphol. and in their ability to agglutinate erythrocytes and elicit high titers of neutralizing antibodies. Protection from tumor challenge was tested in C57BL/6 mice by using the tumor cell line TC-1, which expresses **HPV16** E7, but not the virion structural proteins. Injection of **HPV16** L1/L2-**HPV16** E7 chimeric VLPs, but not **HPV16** L1/L2 VLPs, protected the mice from tumor challenge, even in the absence of adjuvant. The chimeric VLPs also induced protection against tumor challenge in major histocompatibility class II-deficient mice, but not in .beta.2-microglobulin or perforin knockout mice implying that protection was mediated by class I-restricted cytotoxic lymphocytes. These findings raise the possibility that VLPs may generally be efficient vehicles for generating cell-mediated immune responses and that, specifically, chimeric VLPs contg. **papillomavirus** nonstructural proteins may increase the therapeutic potential of VLP-based prophylactic vaccines in humans.

L20 ANSWER 16 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:71229 HCAPLUS
DOCUMENT NUMBER: 128:137193
TITLE: Infectious **papillomavirus** pseudoviral particles, methods for preparing them, and their use in immunization and gene therapy
INVENTOR(S): Lowy, Douglas R.; Schiller, John T.; Roden, Richard B.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Lowy, Douglas R.; Schiller, John T.; Roden, Richard B.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9802548	A2	19980122	WO 1997-US12115	19970714
WO 9802548	A3	19980305		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2257822	AA	19980122	CA 1997-2257822	19970714
AU 9737256	A1	19980209	AU 1997-37256	19970714
EP 922105	A2	19990616	EP 1997-934126	19970714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000515741	T2	20001128	JP 1998-506187	19970714
PRIORITY APPLN. INFO.:			US 1996-22104	19960717
			WO 1997-US12115	19970714

AB The invention provides an infectious **papillomavirus** pseudoviral particle useful in gene transfer comprising: (a) a **papillomavirus** vector DNA which comprises an E2 binding site and an expression cassette comprising a gene and a sequence controlling expression of said gene; and (b) a **papillomavirus** capsid which comprises L1 and L2 structural proteins, such that said capsid encapsidates said vector DNA, wherein said gene is derived from a first biol. species and said **L1** structural **protein** is derived from a second biol. species and said first biol. species is different from said second biol. species. The pseudoviral particles are prepd. by (a) providing a cell line which expresses **papillomavirus E2** DNA binding **protein** and **L1** and L2 structural proteins; (b) transforming the cell line with a **papillomavirus** vector DNA which comprises an E2 binding site and an expression cassette comprising a gene and a sequence controlling expression of the gene; (c) providing conditions for the encapsidation of the vector DNA by a capsid which comprises the L1 and L2 structural proteins to generate the particles; and (d) harvesting the particles. Expts. exploring the role of L2 in the assembly of the pseudoviral particles are described. Infectious **HPV16**(BPV1) virions (i.e., bovine **papillomavirus** 1

genomic DNA encapsidated with human **papillomavirus** 16 L1 and L2 proteins) were prepd. in BPHE-1 (mammalian) cells. Infectious BPV were obtained from Sf9 (insect) cells by transfecting the cells with full-length circular BPV DNA and infecting them with baculoviruses expressing L1, L2 and E2.

L20 ANSWER 17 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:1587 HCAPLUS
DOCUMENT NUMBER: 128:71620
TITLE: Virus-like particles useful as a vector for delivering human **papillomavirus** genes E2 and L1/L2
INVENTOR(S): Bloch, Marie-Aline
PATENT ASSIGNEE(S): Pasteur Merieux Serums Et Vaccins, Fr.; Bloch, Marie-Aline
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746693	A1	19971211	WO 1997-FR962	19970603
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2749323	A1	19971205	FR 1996-7174	19960604
FR 2749323	B1	19980710		
AU 9730980	A1	19980105	AU 1997-30980	19970603
AU 725518	B2	20001012		
EP 910656	A1	19990428	EP 1997-926078	19970603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000511773	T2	20000912	JP 1998-500269	19970603
PRIORITY APPLN. INFO.:			FR 1996-7174	19960604
			WO 1997-FR962	19970603

AB The invention discloses a non-infectious virus-like particle (VLP) comprising (i) a capsid defining an internal space and constituted by all or part of the **L1 protein** and optionally all or part of the **E2 protein** of a human **papillomavirus**, and, (ii) a nucleic acid mol. contained in the said internal space; the nucleic acid mol. comprising a region coding for a protein of interest, in particular an antigen or a cytokine. VLPs encoding chimeric proteins such as L1-E7 and L2-E7 are also claimed. Human **papillomaviruses** 1,6,10,11,16,18, 31, 33, 35, or 45 are claimed. The invention is exemplified by construction of a VLP contg.a **HPV** 16 mutant L1 gene in which the encoded protein contains aspartic acid or glutamic acid in place of histidine at position 202. Proteins such as cytokines, tumor antigens, or T-cell helper recognition proteins can also be encoded by the VLPs. The VLPs also contain the **papillomaviral** locus control region (LCR). Such VLP's can be administered in vivo and are particularly useful for vaccinal purposes in therapy or for prevention against all kinds of cancerous conditions or infections.

L20 ANSWER 18 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:737867 HCAPLUS
DOCUMENT NUMBER: 128:33124

TITLE: Characterization of events during the late stages of **HPV16** infection in vivo using high-affinity synthetic Fabs to E4
AUTHOR(S): Doorbar, John; Foo, Charmaine; Coleman, Nick; Medcalf, Liz; Hartley, Oliver; Prospero, Terence; Napthine, Sawsan; Sterling, Jane; Winter, Greg; Griffin, Heather
CORPORATE SOURCE: National Institute for Medical Research, London, UK
SOURCE: Virology (1997), 238(1), 40-52
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **HPV** late gene expression is initiated as an infected basal cell migrates through the differentiating layers of the epidermis, resulting in the onset of vegetative viral DNA replication and the expression of viral late proteins. The authors have used a large synthetic Ig library displayed on phage (diversity 6.5 .times. 1010 phage) to isolate three Fabs (TVG405, 406, and 407) which recognize distinct epitopes on the **E4** late **protein** of **HPV16**. A C-terminal monoclonal (TVG404) was generated by hybridoma technol., and N-terminal polyclonal antiserum was prepd. by peptide immunization (.alpha. N-term). The most potent antibody (TVG405) had an affinity for E4 of approx. 1.0 nM. All antibodies recognized the protein in paraffin-embedded archival material, allowing the authors to map events in the late stages of virus infection. Expression of E4 in vivo does not coincide with synthesis of the major virus coat **protein L1**, but precedes it by 1 or 2 cell layers in premalignant lesions caused by **HPV16** and by up to 20 cell layers in **HPV63**-induced warts. In higher grade lesions assocd. with **HPV16**, E4 is produced in the absence of L1. By contrast, vegetative viral DNA replication and E4 expression correlate exactly and in some lesions begin as the infected epithelial cell leaves the basal layer. Differentiation markers such as filaggrin, loricrin, and certain keratins are not detectable in E4-pos. cells, and nuclear degeneration is delayed. **HPV16** E4 has a filamentous distribution in the lower epithelial layers, but assocs. with solitary perinuclear structures in more differentiated cells. Antibodies to the N-terminus of the protein stained these structures poorly. The authors' findings are compatible with a role for the **HPV16 E4 protein** in vegetative DNA replication or in modifying the phenotype of the infected cell to favor virus synthesis or virus release. The Fabs will be of value in the evaluation of model systems for mimicking **HPV** infection in vitro.

L20 ANSWER 19 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:567150 HCAPLUS
DOCUMENT NUMBER: 127:259828
TITLE: Sequence variations and viral genomic state of human **papillomavirus** type 16 in penile carcinomas from Ugandan patients
AUTHOR(S): Tornesello, Maria Lina; Buonaguro, Franco M.; Meglio, Antonella; Buonaguro, Luigi; Beth-Giraldo, Elke; Giraldo, Gaetano
CORPORATE SOURCE: Division of Viral Oncology, National Cancer Institute, "Fondazione Pascale", Naples, 1-80131, Italy
SOURCE: J. Gen. Virol. (1997), 78(9), 2199-2208
CODEN: JGVIAY; ISSN: 0022-1317

PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sequence variations in the E6/E7 (nt 34-880) and the L1 (nt 6584-7035) ORFs, and in the long control region (LCR) (nt 7289-93) of human **papillomavirus** type 16 (**HPV**-16) were analyzed in five penile carcinoma biopsies obtained from Ugandan patients. Uganda is a country with a high incidence of genital cancers. All five isolates were classified as members of Africa-1 lineage (Af1) by phylogenetic anal. based on LCR sequences. The E6 gene phylogenetic anal., however, showed that four isolates fell into a new subclass designated Af1-u. This subclass, characterized by three point mutations located at the 5' end of the E6 gene with resulting changes in amino acids at positions 10 and 14, is distinguishable from the Af1 class by the absence of synonymous mutations at nt 286 and 289. The nonsynonymous substitution at nt 335 was present in three out of five samples. The E6 Af1 mutation pattern was present in only a single Ugandan **HPV**-16 isolate. Nucleotide sequence anal. of the E7 and L1 regions did not allow any Af1 subclass identification. The phys. state of the viral DNA in these samples was characterized by PCR and Southern blot anal. Oligonucleotides which enable amplification of the full length E2 region (nt 2734-3872) failed to amplify the target sequence in four out of five samples, suggesting disruption of the E2 ORF and integration of the **HPV** genome into the human DNA. Southern blot anal. confirmed the virus integration status. Our results contribute to the characterization of the **HPV** -16 "African lineages" with the identification of the Af1-u subclass; furthermore, this is also the first report showing that in male genital cancers **HPV**-16 is integrated into the human genome with disruption of the E2 ORF.

L20 ANSWER 20 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:494761 HCAPLUS
DOCUMENT NUMBER: 127:202631
TITLE: Chimeric **papillomavirus**-like particles
AUTHOR(S): Muller, Martin; Zhou, Jian; Reed, Tracey D.; Rittmuller, Claudia; Burger, Alexander; Gabelsberger, Josef; Braspenning, Joris; Gissmann, Lutz
CORPORATE SOURCE: Department of Microbiology and Immunology, Loyola University Chicago, Maywood, IL, 60153, USA
SOURCE: Virology (1997), 234(1), 93-111
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chimeric **papillomavirus**-like particles (CVLPs) were constructed by replacing the 34 carboxy-terminal amino acids of the human **papillomavirus** (**HPV**) 16 **L1 protein** with various parts of the **HPV** 16 **E7 protein**. Chimeric proteins were expressed by recombinant baculoviruses and analyzed by electron microscopy for their ability to assemble into virus capsids. CVLPs were produced in high efficiencies with inserts of .ltoreq.60 amino acids. CVLPs induce a neutralizing antibody response, assayed by inhibition of hemagglutination of mouse erythrocytes. CVLPs interact with the putative receptor for **papillomaviruses**, as they hemagglutinated mouse red blood cells and bound to and penetrated cells in vitro. As CVLPs follow a similar intracellular pathway as obsd. earlier

for bovine **papillomavirus** VLPs, CVLPs may be used to deliver peptides into mammalian cells in vitro and in vivo, possibly reaching the pathway for MHC class I presentation.

L20 ANSWER 21 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:484298 HCAPLUS
DOCUMENT NUMBER: 125:160215
TITLE: Virus-like particles and **E1-E4 protein** expressed from the human **papillomavirus** type 11 bicistronic E1-E4-L1 transcript
AUTHOR(S): Brown, Darron R.; Pratt, Linda; Bryan, Janine T.; Fife, Kenneth H.; Jansen, Kathrin
CORPORATE SOURCE: Dep. Med., Microbiology and Immunology and Pathology, Indiana Univ. Sch. Med., Indianapolis, IN, 46202, USA
SOURCE: Virology (1996), 222(1), 43-50
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Detection of **E1-E4 protein** in human **papillomavirus** (**HPV** 11)-infected tissue is tightly linked to detection of **L1** major capsid **protein**. The only L1-contg. transcript identified in **HPV** 11-infected tissue is the bicistronic E1-E4-L1 mRNA, potentially encoding both the E1-E4 and the L1 proteins. It has not been established that these proteins can be expressed from the E1-E4-L1 transcript. The **HPV** 11 E1-E4-L1 sequence was cloned by reverse transcriptase polymerase chain reaction into the p1393 vector to produce recombinant baculoviruses. Immunoblots of recombinant baculovirus-infected Sf9 cell lysates demonstrated both the E1-E4 and the L1 proteins. An ELISA was performed on infected Sf9 cells using a monoclonal antibody specific for nondenatured L1, demonstrating that 10 ng of native **L1 protein** was present per .mu.g of total nuclear protein. Electron microscopic anal. revealed 50- to 60-nm icosahedral virus-like particles. In vitro transcription/translation was performed using pSPORT constructs contg. the E1-E4-L1 sequence or, as controls, monocistronic pSPORT-E1-E4 or L1 constructs. The pSPORT-E1-E4-L1 construct produced the E1-E4 and L1 proteins at a ratio of 17:1. For **E1-E4 protein**, expression was greater from the pSPORT-E1-E4-L1 construct than from the monocistronic pSPOR-E1-E4 construct. In contrast, more **L1 protein** was expressed from pSPORT-L1 than from pSPORT-E1-E4-L1. A mutant E1-E4-L1 construct contg. no E1-E4 start codon expressed **L1 protein** in amts. nearly equal to that expressed from the pSPORT-L1 construct. Addn. of an antisense oligonucleotide directed at the E1-E4 start codon region to in vitro reactions using pSPORT-E1-E4-L1 was assocd. with inhibition of **E1-E4 protein** synthesis and increased translation of **L1 protein**.

L20 ANSWER 22 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:150324 HCAPLUS
DOCUMENT NUMBER: 124:200195
TITLE: Polynucleotide vaccine for **papillomavirus**
INVENTOR(S): Donnelly, John J.; Liu, Margaret A.; Martinez, Douglas; Montgomery, Donna L.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9600583	A1	19960111	WO 1995-US6915	19950601
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526945	A1	19960125	AU 1995-26945	19950601
AU 701973	B2	19990211		
EP 768893	A1	19970423	EP 1995-922160	19950601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1156966	A	19970813	CN 1995-194672	19950601
HU 76446	A2	19970929	HU 1996-3562	19950601
JP 10501987	T2	19980224	JP 1995-503166	19950601
ZA 9504641	A	19960126	ZA 1995-4641	19950606
US 5866553	A	19990202	US 1996-750810	19961217
FI 9605224	A	19961227	FI 1996-5224	19961227
NO 9605590	A	19970228	NO 1996-5590	19961227
PRIORITY APPLN. INFO.:			US 1994-268424	19940630
			WO 1995-US6915	19950601

AB DNA constructs encoding **papilloma** virus gene products, capable of being expressed upon direct introduction into animal tissues are novel prophylactic pharmaceuticals which can provide immune protection against infection by **papilloma** virus. In example, plasmids encoding cottontail rabbit **papilloma** virus **protein L1**, L2, **E2**, E4, or E7 were constructed, purified, and tested for induction of specific antibodies and for protection of rabbits from infected by **papillomavirus**.

L20 ANSWER 23 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:977576 HCAPLUS
DOCUMENT NUMBER: 124:50298
TITLE: Human **papillomavirus** type 11 E1.cxa.E4 and L1 proteins colocalize in the mouse xenograft system at multiple time points
AUTHOR(S): Brown, Darron R.; Bryan, Janine T.; Pratt, Linda; Handy, Victoria; Fife, Kenneth H.; Stoler, Mark H.
CORPORATE SOURCE: Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, 46202, USA
SOURCE: Virology (1995), 214(1), 259-63
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The most abundant viral mRNA species in **HPV** 11-infected tissue consists of two exons, joining a segment of open reading frame (ORF) E1 to ORF E4, potentially encoding the **E1**.cxa.**E4** **protein**. The L1 ORF encodes the major capsid protein of

HPV. Our previous studies demonstrated colocalization of the **HPV** 11 E1.cxa.E4 and L1 proteins within the same cells of **HPV** 11-infected foreskin implants grown in athymic mice (the mouse xenograft system) and removed 12 wk after implantation. Prior studies have demonstrated E1.cxa.E4 transcripts early in infection and throughout the **HPV** 11-infected epithelium, while L1 transcripts are detected later, and in a subset of E1.cxa.E4 mRNA-pos. differentiated epithelial cells. Therefore, **E1**.cxa.**E4 protein** may be produced at an earlier time point or in less differentiated cells than the **L1 protein**. To study these questions, athymic mice were implanted with **HPV** 11-infected human foreskin fragments. Mice were sacrificed at 1-wk intervals beginning 2 wk after implantation of tissue. The E1.cxa.E4 and L1 proteins colocalized to the same differentiated epithelial cells or to tight clusters of cells in differentiated epithelial layers of **HPV** 11-infected implants. The E1.cxa.E4 and L1 proteins were first detected 4 wk after implantation. **E1**.cxa.**E4 protein** was detected in the region of the cell membrane and cytoplasm, and never in the nucleus. **L1 protein** was only detected in the nucleus. Both proteins were detected in implants contg. high viral copy nos. No specific histol. changes were uniformly assocd. with detection of these proteins. The tight coupling of the E1.cxa.E4 and L1 proteins at multiple time points suggests that expression of both proteins is necessary to complete the virus life cycle.

L20 ANSWER 24 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:241948 HCAPLUS
DOCUMENT NUMBER: 120:241948
TITLE: Human **papillomavirus** type 16 E6, E7 and L1 and type 18 E7 proteins produced by recombinant baculoviruses
AUTHOR(S): Park, David S.; Selvey, Linda A.; Kelsall, Stephen R.; Frazer, Ian H.
CORPORATE SOURCE: Lions Human Immunol. Lab., Univ. Queensland, Woolloongabba, 4102, Australia
SOURCE: J. Virol. Methods (1993), 45(3), 303-18
CODEN: JVMEDH; ISSN: 0166-0934
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Proteins derived from the E6, E7 and L1 ORFs of **HPV16** and the E7 ORF of **HPV18** were produced in insect cells using a baculovirus expression system. **HPV** ORFs were inserted into baculovirus transfer vectors pAcYM1 or pVL1393/2, and recombinant baculoviruses isolated using a combination of limiting diln. and plaque assay. Using **HPV**-specific antisera and monoclonal antibodies **HPV** proteins were identified in lysates of Spodoptera frugiperda (Sf-21) cells infected with **HPV**-recombinant baculovirus. Immunoreactive **HPV16 E7 protein** produced in Sf-21 cells had an apparent Mr of 19 kDa, larger than that predicted from the amino acid sequence, and similar to that of native **HPV16 E7 protein** in HeLa and CaSki cells. The apparent Mr of recombinant **HPV18**-E7, **HPV16**-L1 and **HPV16**-E6 proteins was equiv. to the Mr values predicted from the amino acid sequence. Thermostability studies revealed that the half-life of **HPV16-E7 protein** in Sf-21 cell lysate was approx. 20 h at 4, and less than 30 min at 37. **HPV16** L1, **HPV16** E7 and

HPV18 E7 proteins were predominantly localized in the nucleus of recombinant baculovirus-infected Sf-21 cells, whereas recombinant **HPV** 16 **E6 protein** was localized in both the cytoplasm and nucleus of infected insect cells. Northern blot anal. of RNA derived from insect cells infected with vAc16E6E7, a recombinant baculovirus contg. both **HPV16** E6 and E7 ORF's, revealed the presence of only E6 ORF transcripts, suggesting that the splicing of RNA products derived from the E6 and E7 ORF's, as obsd. in cervical cancer-derived cell lines, is not performed in insect cells. Baculovirus-derived **HPV** proteins have similar biol. properties to the native proteins and should be suitable for studies on the immunol. of **HPV**.

L20 ANSWER 25 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:161025 HCAPLUS
DOCUMENT NUMBER: 120:161025
TITLE: Delayed-type hypersensitivity response to human **papillomavirus** type 16 **E6 protein** in a mouse model
AUTHOR(S): Chambers, Mark A.; Stacey, Simon N.; Arrand, John R.; Stanley, Margaret A.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, CB2 1QP, UK
SOURCE: J. Gen. Virol. (1994), 75(1), 165-9
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A mouse model incorporating the epitheliotropic nature of human **papillomavirus** (**HPV**) infections has been used to study an immune response to **HPV** type 16 (**HPV**-16) **E6 protein** in vivo. Using a transplantation technique, a novel immortal keratinocyte cell line expressing the **E6 protein** was grafted onto syngeneic mice to re-form a differentiated epithelium overlying a granulation tissue bed. By this approach the presentation of viral antigens to the immune system can be modelled in a way analogous to the natural infection. Here the authors report a delayed-type hypersensitivity (DTH) reaction in grafted mice challenged intradermally with a recombinant vaccinia virus expressing the **HPV**-16 **E6 protein**. The specificity of the response was confirmed by the absence of a DTH reaction to challenge with virus expressing either **HPV**-167 **E7** or **L1 protein**.

L20 ANSWER 26 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:49805 HCAPLUS
DOCUMENT NUMBER: 120:49805
TITLE: Translational properties of the human **papillomavirus** type-6 L1-coding mRNA
AUTHOR(S): Tomita, Yoshimi; Simizu, Bunsiti
CORPORATE SOURCE: Sch. Med., Chiba Univ., Chiba, 260, Japan
SOURCE: Gene (1993), 133(2), 223-5
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A cDNA encoding a bicistronic mRNA, E1.cxa.E4.cxa.L1, which was generated by double-splicing of the E1, E4 and L1 genes of type-6 human **papillomavirus** (**HPV**-6), was cloned. The E1.cxa.E4 and

L1 open reading frames (ORFs) in this cDNA were expressed in COS-1 or CV-1 cells as fusion proteins with Escherichia coli .beta.-galactosidase (.beta.Gal), and the products were analyzed by immunopptn. and enzyme assay. The results showed that the translational efficiency of the L1 ORF was about 9-15-fold less efficient than that of the E1.cxa.E4 ORF. Substitution of the ATG of the E1.cxa.E4 ORF with AAG increased translation of the L1 ORF about 30-fold. Lengthening of the intercistronic sequence to 31 bp, equiv. in length to the bicistronic **HPV**-1 mRNA, showed little translational effect relative to the wild-type 12-bp intercistronic sequence. (Carets [.cxa.] represent splicing of RNA.).

L20 ANSWER 27 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:425591 HCAPLUS
DOCUMENT NUMBER: 119:25591
TITLE: Immunoelectron microscopical localization of human **papillomavirus** type 16 L1 and E4 proteins in cervical keratinocytes cultured in vivo
AUTHOR(S): Sterling, Jane C.; Skepper, Jeremy N.; Stanley, Margaret A.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: J. Invest. Dermatol. (1993), 100(2), 154-8
CODEN: JIDEAE; ISSN: 0022-202X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human **papillomavirus** (**HPV**) causes warts, but is also assocd. with the development of squamous cell dysplasia and carcinoma. The virus is host and tissue specific and the numerous **HPV** types show a predilection for different body sites. Exptl. prodn. of **HPV** 16 particles is at present only possible using in vivo culture of keratinocytes contg. episomal viral DNA. Using immunoelectron microscopy, the authors have investigated the localization of **HPV** 16 E4 and L1 proteins in a keratinized epithelium formed by grafting **HPV** 16-contg. cervical keratinocytes onto the athymic mouse. New viral progeny are produced in this system, as confirmed by labeling of intranuclear particles with a mouse monoclonal antibody against the **HPV** 16 major capsid (**L1**) **protein**. The role of the **E4 protein** is not yet clear, although it is believed to be important for the later stages of the virus life cycle. Its cytoplasmic localization is confirmed in the cells of the spinous and granular layers and demonstrate co-localization with keratin tonofilaments.

L20 ANSWER 28 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:37211 HCAPLUS
DOCUMENT NUMBER: 118:37211
TITLE: Induction of cytotoxic T lymphocytes with peptides in vitro: Identification of candidate T-cell epitopes in human **papilloma** virus
AUTHOR(S): Strauss, Hans J.; Davies, Huw; Sadovnikova, Elena; Chain, Benny; Horowitz, Neil; Sinclair, Christine
CORPORATE SOURCE: Imp. Cancer Res. Fund, Univ. Coll., London, UK
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1992), 89(17), 7871-5
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A set of overlapping peptides corresponding to the L1, E6, and E7 proteins of human **papilloma** virus 16 was tested for their ability to bind to major histocompatibility complex class I mols. and to stimulate cytotoxic T-lymphocyte (CTL) responses in vitro. A class I binding assay using intact RMA-S cells showed that 20 of the 99 human **papilloma** virus peptides bound to H-2Kb and/or Db mols. Fifteen of the 20 class I-binding peptides stimulated primary CTL responses, whereas peptides that were neg. in the binding assay failed to do so. Peptide-induced CTLs recognized the immunizing peptide very efficiently, requiring no more than 1-10 nM peptide for target cell lysis. However, 2 observations were made that have important implications for the design of peptide-based vaccines for inducing CTLs. Not all major histocompatibility complex-binding peptides that contained known motifs characteristic of naturally processed peptides induced CTLs. The efficiency of CTL lysis was strongly decreased when the size of the target peptide differed by only 1 amino acid residue from that of the immunizing peptide. Thus, peptides chosen for vaccination must correspond in length to naturally processed peptides.

L20 ANSWER 29 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:606045 HCAPLUS
DOCUMENT NUMBER: 117:206045
TITLE: Human **papillomavirus** type 58 DNA sequence
AUTHOR(S): Kirii, Yasuyuki; Iwamoto, Seiichi; Matsukura, Toshihiko
CORPORATE SOURCE: Kanebo Inst. Cancer Res., Osaka, 534, Japan
SOURCE: Virology (1991), 185(1), 424-7
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complete nucleotide sequence of human **papillomavirus** type 58 (**HPV** 58) DNA cloned from an invasive cervical carcinoma was detd. The **HPV** 58 genome consists of 7824 nucleotides, contg. 37.9% of GC residues, and has a similar genome organization of other **HPVs**. On the nucleotide sequence level, it conserves the signal sequences for regulation of gene expression as with other genital **HPVs** and exhibits an extensive homol. with **HPV** 33 (77%). Comparative anal. of amino acid sequences reveals that **HPV** 58 is closely related to **HPVs** 16, 31, and 33, and is more distantly related to **HPVs** 6, 11, 18, and 39. **HPVs** 58, 16, 31, and 33 can be regarded as a group in **HPV**.

L20 ANSWER 30 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:192475 HCAPLUS
DOCUMENT NUMBER: 116:192475
TITLE: Seroreactive epitopes of human **papillomavirus** (**HPV**) 16 proteins
INVENTOR(S): Mueller, Martin; Gissmann, Lutz
PATENT ASSIGNEE(S): Behringwerke A.-G., Germany
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 451550	A2	19911016	EP 1991-104197	19910319
EP 451550	A3	19911106		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2038581	AA	19910921	CA 1991-2038581	19910319
AU 9173515	A1	19910926	AU 1991-73515	19910319
AU 650868	B2	19940707		
JP 04217998	A2	19920807	JP 1991-81596	19910320
PRIORITY APPLN. INFO.:			EP 1990-105222	19900320

AB Seroreactive epitopes of **HPV16** proteins E4, E6, E7, and L1 are identified. Also provided are peptides contg. these epitopes. The peptides of the invention are useful for a vaccine and a diagnostic kit. Epitope and peptide sequences are included.

L20 ANSWER 31 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:52489 HCAPLUS
DOCUMENT NUMBER: 116:52489
TITLE: Biologic properties and nucleotide sequence analysis of human **papillomavirus** type 51
AUTHOR(S): Lungu, Octavian; Crum, Christopher P.; Silverstein, Saul
CORPORATE SOURCE: Dep. Microbiol., Columbia Univ., New York, NY, 10032, USA
SOURCE: J. Virol. (1991), 65(8), 4216-25
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human **papillomaviruses** (**HPVs**) may be grouped according to the site from which they are isolated and the disease with which they are assocd. **HPV** type 51 (**HPV**-51) was recently cloned from a low-grade precancerous lesion (G. Nuovo, et al., 1988). Mol. epidemiol. anal. of cervical lesions, including condylomata and low- and high-grade precancers, revealed that **HPV**-51 was present in .apprx.5% of the samples examd. The complete nucleotide sequence of this virus was detd. and compared with other sequenced **HPVs**. Anal. reveals that the 7808-bp genome is composed of 8 open reading frames which ar encoded on the same strand and that this virus is most closely related to **HPV**-31. Sequence comparisons place this virus in the group of high-risk viruses (those with an increased risk of progressing to malignancy) along with **HPV**-16, -18, -31, and -33. Morphol. transformation expts. demonstrated that **HPV**-51 had transformation potential and that transformed cells contained RNAs homologous to E6 and E7.

L20 ANSWER 32 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:624933 HCAPLUS
DOCUMENT NUMBER: 115:224933
TITLE: A subtype of human **papillomavirus** 5 (**HPV**-5b) and its subgenomic segment amplified in a carcinoma: nucleotide sequences and genomic organizations
AUTHOR(S): Yabe, Yoshiro; Sakai, Akiko; Hitsumoto, Takako; Kato, Hiroko; Ogura, Hajime
CORPORATE SOURCE: Med. Sch., Okayama Univ., Okayama, 700, Japan
SOURCE: Virology (1991), 183(2), 793-8
CODEN: VIRLAX; ISSN: 0042-6822

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A subtype of human **papillomavirus** 5 (**HPV**-5b) is closely assocd. with carcinomas in the disease epidermodysplasia verruciformis (EV). The complete genome was cloned from virus particles in benign lesions of a patient with EV and sequenced: it was 7779 nucleotides long and consisted of 6 open reading frames (ORFs) (E6, E7, E1, E2, E4, and E5) in the early region, 3 ORFs (L2, L3, and L1) in the late region, and a noncoding region, all existing on one DNA strand. The 40% segment of the **HPV**-5b genome specifically amplified in carcinomas was cloned from a primary carcinoma of the same EV patient and sequenced: it was 3143 nucleotides long and corresponded to a segment of the original **HPV**-5b genome contg. the entire sequences of E6, E7, and the noncoding region and portions of E1 and L1. Compared to the whole genomic DNA, no mutations were detected in this probable malignancy-assocd. viral subgenomic segment cloned from carcinoma. These results suggest that amplification of the viral segment contg. E6, E7, and the noncoding region may play a role in the malignant conversion of **HPV**-5b-infected benign lesions and that mutations in these genes or regions are not necessarily required.

L20 ANSWER 33 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:552082 HCAPLUS
DOCUMENT NUMBER: 115:152082
TITLE: Nucleotide and amino acid sequence variation in the L1 and E7 open reading frames of human **papillomavirus** type 6 and type 16
AUTHOR(S): Icenogle, Joseph P.; Sathya, Pushpa; Miller, Donna L.; Tucker, Ruth Ann; Rawls, William E.
CORPORATE SOURCE: Div. Viral Rickettsial Dis., Cent. Dis. Control, Atlanta, GA, 30333, USA
SOURCE: Virology (1991), 184(1), 101-7
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human **papillomavirus** (**HPV**) type 6 and type 16 DNA sequence variants were found by partially sequencing the L1 and E7 open reading frames, using templates generated with the polymerase chain reaction. Identical variants were found in patients from widely sepd. locations, such as the United States, the Philippines, and India. The same sequence variants of **HPV** 16 were found in women with invasive cervical carcinoma and in women with no evidence of disease. Variation in the predicted amino acid sequences of the **HPV** 16 L1 and E7 proteins was found. A single nucleotide change at position 6433 was found in about 50% of the **HPV** 16 DNAs, resulting in a change in predicted amino acid sequence from threonine to alanine at the equiv. position in the **L1 protein**. Predicted amino acid changes were found in the **HPV** 16 E7 proteins at amino acid positions 28, 29, and 47. Variation at these positions could affect known properties of the **E7 protein**, including binding to the retinoblastoma protein.

L20 ANSWER 34 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:406038 HCAPLUS
DOCUMENT NUMBER: 115:6038
TITLE: Molecular biologic study on the carcinogenesis of

HPV in uterine cervical cancer and related lesions. Analysis of **HPV** types 16, 18 E6/E7 gene mRNA

AUTHOR(S): Nagai, Nobutaka
CORPORATE SOURCE: Sch. Med., Hiroshima Univ., Hiroshima, Japan
SOURCE: Nippon Sanka Fujinka Gakkai Zasshi (1990), 42(8), 823-33
CODEN: NISFAY; ISSN: 0300-9165
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB In order to investigate the relationship between human **papillomavirus** (**HPV**) DNA and cervical cancer, the authors studied the involvement of **HPV** in cervical cancer and related lesions by dot blot hybridization (D.B.H.), Southern blot hybridization (S.B.H.), in situ hybridization (I.S.H.) and polymerase chain reaction (P.C.R.). Some **HPV** DNA and mRNA pos. or neg. cases of cervical dysplasia were followed for more than 16 mo prospectively. **HPV** DNA were detected in cervical dysplasia and cancer and **HPV** pos. rate increased as the grade of cervical dysplasia became higher by several mol. biol. analyses. I.S.H. with biotinylated **HPV** DNA probes revealed that **HPV** DNA was located in the nuclei of koilocytosis, dysplastic cells and cancer cells. In anal. of **HPV** type in squamous epithelium, **HPV** 6/11 had the highest pos. rate (21.1%) in mild dysplasia. On the other hand, **HPV16** pos. rate increased with the grade of dysplasia and 34.9% (15/42) of moderate dysplasia and 51.4% (18/35) of severe dysplasia were pos. for **HPV** 16 DNA, resp. The N/C ratio in **HPV** 16 pos. cells was increased. These findings suggest that **HPV** 16 is assocd. with squamous epithelial neoplasia. About 50% of metaplasia close to cervical neoplasia with **HPV** DNA was pos. for the same type of **HPV**. In columnar epithelium, several types of **HPV** DNA were detected in 46.7% (15/32) of cervical adenocarcinoma. Thirty one percent (10/32) of adenocarcinoma, 50% (4/8) of adenosquamous cell carcinomas were pos. for **HPV** 18. This suggests an assocn. between **HPV** 18 and adenocarcinoma and related lesions. The authors examd. amplified DNA detection of **HPV** 16 and 18 E7 gene by P.C.R. method. **HPV** 16 and/or 18 DNA were detected in 25 of 43 cases of cervical scrapes obtained from cervical neoplasia. On immunohistochem. and mol. biol. studies there was no correlation between **HPV** DNA and c-myc product and c-myc gene amplification. The early genes E6/E7 of **HPV** 16 and 18 were considered as one of the carcinogenic factors of uterine cervix. The localization of **HPV** E6/E7 and L1/L2 mRNA in cervical dysplasia and CIS with I.S.H. was studied using antisense and sense biotinylated **HPV** RNA probes which were made by in vitro transcription. E6/E7 and L1/L2 mRNA were obsd. in the cytoplasm and nuclei of the dysplastic cells or cancer cells of **HPV** DNA pos. cases by antisense **HPV** E6/E7 or L1/L2 RNA probe. The persistent or progressive rate of cervical dysplasia increased in **HPV** DNA pos. cases compared with **HPV** DNA neg. cases in the follow up study. In **HPV** DNA pos. cases, esp. cervical dysplasia which **HPV** 16 DNA and E6/E7 mRNA were detected significantly progressed in CIS. On the other hand, many cases of cervical dysplasia which were pos. for **HPV** L1/L2 mRNA regress to the low grade of cervical neoplasia. It was concluded that differences in **HPV** E6/E7 and L1/L2 gene expression were very important in the development of cervical dysplasia in the follow up study. These findings

suggest that there is an assocn. between DNA detection and E6/E7 gene expression of **HPV** in high risk groups and cervical carcinogenesis.

L20 ANSWER 35 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:402028 HCAPLUS
DOCUMENT NUMBER: 115:2028
TITLE: Nucleotide sequence of human **papillomavirus** (**HPV**) type 41: an unusual **HPV** type without a typical E2 binding site consensus sequence
AUTHOR(S): Hirt, Lorenz; Hirsch-Behnam, Anja; De Villiers, Ethel Michele
CORPORATE SOURCE: Referenzzent. Humanpathog. Papillomviren, Dtsch. Krebsforschungszent., Heidelberg, 6900, Fed. Rep. Ger.
SOURCE: Virus Res. (1991), 18(2-3), 179-89
CODEN: VIREDF; ISSN: 0168-1702
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complete nucleotide sequence of human **papillomavirus** type 41 (**HPV**-41) has been detd. **HPV**-41 was originally isolated from a facial wart, but its DNA has subsequently been detected in some skin carcinomas and premalignant keratoses (Grimmel, M., et al., 1988, and E.-M. de Villiers, M. Grimmel, and C. Neumann, unpublished results). Anal. of the cloned **HPV**-41 nucleic acid reveals that its genome organization is similar to that of other **papillomavirus** types. Yet, the anal. indicates at the same time that this virus is most distantly related to all other types of human-pathogenic **papillomaviruses** sequenced thus far and appears to identify **HPV**-41 as the first member of a new subgroup of **HPV**. The overall nucleotide homol. to other sequenced **HPV** types is below 50%. The closest other **HPV** type is represented by **HPV**-18, sharing 49% identical nucleotides. The typical E2-binding sequence ACCN6GGT, found in all **papillomaviruses** analyzed to date, does not occur in the upper regulatory region of the **HPV** -41 genome. Modified E2-binding sequences, as described for BPV 1 (Li, R., et al., 1989), are located in the domain proximal to the E6 ORF. These are ACCN6GTT, AACN6GGT and the 2 perfect palindromic sequences AACGAATTCGTT.

L20 ANSWER 36 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:179143 HCAPLUS
DOCUMENT NUMBER: 114:179143
TITLE: Genome organization and nucleotide sequence of human **papillomavirus** type 39
AUTHOR(S): Volpers, Christoph; Streeck, Rolf E.
CORPORATE SOURCE: Inst. Med. Mikrobiol., Johannes Gutenberg-Univ., Mainz, D-6500, Fed. Rep. Ger.
SOURCE: Virology (1991), 181(1), 419-23
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 7833-bp nucleotide sequence of human **papillomavirus** type 39 (**HPV39**), which is assocd. with genital intraepithelial neoplasias and invasive carcinomas, was detd. The genome organization deduced from the sequence shares characteristic features with other

genital **papillomaviruses**. According to sequence comparisons, **HPV39** most closely resembles **HPV18** and may be a member of a subgroup of genital **papillomaviruses** distinct from the **HPV16**/31/33 group. As a novel feature, a 1.3-kb open reading frame on the DNA strand is reported which lacks major open reading frames in the other sequenced **HPV** genomes.

L20 ANSWER 37 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:527346 HCAPLUS
DOCUMENT NUMBER: 113:127346
TITLE: Detection of novel splicing patterns in a **HPV16**-containing keratinocyte cell line
AUTHOR(S): Doorbar, J.; Parton, A.; Hartley, K.; Banks, L.; Crook, T.; Stanley, M.; Crawford, L.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, CB2 1QP, UK
SOURCE: Virology (1990), 178(1), 254-62
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The W12 cell line was derived from a low grade cervical lesion, and is unique among human **papillomavirus** type 16 (**HPV16**)-contg. cell lines in carrying its **HPV16** genome as a multicopy episome. As such it is thought to be more representative of a premalignant **HPV16**-induced tumor than the cervical cancers from which other cell lines have been derived. Using the polymerase chain reaction (PCR), a no. of novel cDNA species, which appear to be characteristic of the W12 cell line, were identified and cloned. Two species were identified with E6* coding capacity (E6*I and E6*III). The smaller of these (1009 bp) was predicted to encode a novel E6*III polypeptide contg. C-terminal amino acids derived from an out of frame region of the E2/E4 ORFs. The larger species (1480 bp) contained, in addn. to the E6*I ORF, an intact E7 ORF and probably represents the transcript for E7 expression, as the **E7 protein** was readily detectable in the W12 cell line. Both species appeared to be transcribed from the p97 promoter which has been shown to be active in other cell lines. A putative E2 repressor cDNA (891 bp), an E1/E4 message (883 bp), and two novel late cDNA species (1757 and 2031 bp) were also detected, allowing the identification of a splice acceptor immediately in front of the L1 open reading frame (nt 5637) and a splice donor at nt 3631. Although the 1757-base species has the capacity to encode a full-length **L1 protein**, both messages use a splice donor at nt 1301, and are thus not analogous to late species previously identified in **HPV11**. Of the six cDNAs cloned, only the 1480-bp E7 message has been obsd. in other **HPV16**-contg. cell lines. The presence of L1 transcripts, and an E2 repressor mRNA, although unexpected, may reflect the different origins of the W12 cell line.

L20 ANSWER 38 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:527345 HCAPLUS
DOCUMENT NUMBER: 113:127345
TITLE: Coexpression of the human **papillomavirus** type 16 E4 and L1 open reading frames in early cervical neoplasia
AUTHOR(S): Crum, Christopher P.; Barber, Shannon; Symbula, Millie; Snyder, Kim; Saleh, Abdel M.; Roche, James K.
CORPORATE SOURCE: Health Sci. Cent., Univ. Virginia, Charlottesville,

VA, 22908, USA
SOURCE: Virology (1990), 178(1), 238-46
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although the E4 open reading frame (ORF) of human **papillomaviruses** (**HPV**) encodes an abundant protein in cutaneous warts, the location and extent of **HPV** E4 expression in genital precancers, specifically those assocd. with **HPV**-16, has not been described. Expression plasmids (pATH) contg. segments of the **HPV**-16 E4 (3401-3620) and L1 (6151-6792) open reading frames (ORFs) were induced and expressed in bacteria and the resulting fusion proteins were used to elicit antisera in rabbits. Antisera reacting to the E4 and L1 components of the fusion proteins were used to screen biopsies from 150 cervical precancers (cervical intraepithelial neoplasia) and condylomata. Six biopsies exhibited specific immunostaining with the anti-E4 sera. Staining was cytoplasmic, and occurred virtually always in foci contg. immunostaining for L1 proteins. Moreover, anal. of these 6 cases and 22 others for **HPV**-16 RNA by RNA-RNA in situ hybridization demonstrated a similar correlation between E4 immunostaining and the presence of abundant transcripts specific to **HPV**-16. These data are consistent with the hypothesis that expression of the **HPV**-16 E4 ORF is dependent upon viral replication and epithelial differentiation, similar to L1 expression, and that E4 epitopes identified by the rabbit antisera may be unique to **HPV**-16 relative to other common cervical **papillomaviruses**.

L20 ANSWER 39 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:527292 HCAPLUS
DOCUMENT NUMBER: 113:127292
TITLE: Genome organization and taxonomic position of human **papillomavirus** type 47 inferred from its DNA sequence
AUTHOR(S): Kiyono, Tohru; Adachi, Ayumi; Ishibashi, Masahide
CORPORATE SOURCE: Aichi Cancer Cent., Res. Inst., Nagoya, 464, Japan
SOURCE: Virology (1990), 177(1), 401-5
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complete nucleotide sequence of human **papillomavirus** type 47 (**HPV**-47) DNA isolated from the lesion of epidermodysplasia verruciformis (EV) was detd. The computer-aided comparison of **HPV** -47 with other EV-assocd. viruses using the available sequence data on them revealed that **HPV**-47 resembles both **HPV**-8 as much as **HPV**-5 and **HPV**-8 resemble each other, and it suggests these 3 viruses as one cluster and **HPV**-19 and **HPV**-25 as another. The conclusion implies that HPB-47 as well as **HPV5** and **HPV**-8 is assocd. with the cancer occurrence in EV. Two sets of splicing donor and acceptor sequences in **HPV** -47, which were previously shown to work in vivo, are also conserved in **HPV**-5 and **HPV**-8. One of them allows formation of an ORF predicted to encode an **E1/E4** fused **protein**.

L20 ANSWER 40 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:475795 HCAPLUS
DOCUMENT NUMBER: 113:75795

TITLE: Infectious cycle of human **papillomavirus** type 11 in human foreskin xenografts in nude mice
AUTHOR(S): Stoler, Mark H.; Whitbeck, April; Wolinsky, Steven M.; Broker, Thomas R.; Chow, Louise T.; Howett, Mary K.; Kreider, John W.
CORPORATE SOURCE: Sch. Med., Univ. Rochester, Rochester, NY, 14642, USA
SOURCE: J. Virol. (1990), 64(7), 3310-18
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The first mol. anal. of a time course of infection by a **papillomavirus** is reported. The Hershey isolate of the human **papillomavirus** type 11 was used to infect human foreskin tissues, which were then implanted under the renal capsules of nude mice. The xenografts were recovered every 2 wk for 14 wk, fixed in formalin, and embedded in paraffin. Four-micrometer serial sections were examd. by light microscopy for morphol. changes, by immunocytochem. for virion antigen prodn., and by in situ hybridization with 3H-labeled RNA probes for viral DNA replication and expression of the major mRNA species. After a lag period, probes spanning the E4 and E5 open reading frames, which are present in all E region viral mRNAs, generated the first detectable signals at week 4. Signals of other E region probes were minimally detected at week 6. Between weeks 6 and 8, there was an abrupt change in the implant such that cellular proliferation, viral DNA replication, and E and L region mRNA transcription were robust and reached a plateau. By weeks 10 to 12, the exptl. condylomata were morphol. and histol. indistinguishable from naturally occurring condylomata acuminata. These findings suggest that cellular hyperproliferation and the morphol. features of condylomata are direct results of viral genetic activities. Unlike other DNA viruses, the E region transcripts increased with cell age and cellular differentiation and persisted throughout the entire expt. In particular, the mRNA encoding the E1i.cxa.E4 and perhaps E5 proteins remained overwhelmingly abundant. In contrast, viral DNA replication, L region mRNA synthesis, and virion antigen prodn. were restricted to the most differentiated, superficial cells.

L20 ANSWER 41 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:453290 HCAPLUS
DOCUMENT NUMBER: 113:53290
TITLE: Human **papillomavirus** type 1 produces redundant as well as polycistronic mRNAS in plantar warts
AUTHOR(S): Palermo-Dilts, Deborah A.; Broker, Thomas R.; Chow, Louise T.
CORPORATE SOURCE: Sch. Med. Dent., Univ. Rochester, Rochester, NY, 14642, USA
SOURCE: J. Virol. (1990), 64(6), 3144-9
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human **papillomavirus** type 1 (**HPV**-1) causes plantar warts. On the basis of previously mapped mRNAs and sequence homologies of **HPV**-1 to other **papillomaviruses**, the authors designed oligonucleotide primers and employed the polymerase chain reaction to recover **HPV**-1 cDNAs from plantar warts. Seven spliced RNA species were characterized, including three not previously detected, and

the coding potentials of each were deduced. The most abundant viral mRNA encodes an E1i **E4 protein**. One new species is predicted to encode the full-length **E2 protein**, and another can, theor., encode the E2-C or E1-M proteins, three products that regulate mRNA transcription and DNA replication. One RNA species originating from a novel **HPV** promoter in the upstream regulatory region has the potential to encode the minor capsid protein L2. A newly reorganized E5a open reading frame (ORF) is contained in all mRNAs that are polyadenylated at the E-region poly(A) site and also in a putative L2 mRNA. Three distinct species, two of which are derived from the upstream regulatory region promoter, have the potential to encode the **L1 protein**; the third species also contains the entire coding region of the E1i **E4 protein** 5' to the L1 ORF. Both the E1i E4 mRNA and the potentially bicistronic L1 mRNA are derived from a promoter located in the E7 ORF. The authors uncovered no evidence of alternatively spliced mRNAs that could account for the multiple, abundant E4 proteins in plantar warts, suggesting that posttranslational modification is mainly responsible for the obsd. protein heterogeneity.

L20 ANSWER 42 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:214980 HCAPLUS
DOCUMENT NUMBER: 112:214980
TITLE: Human T cell responses to human **papillomavirus** type 16 L1 and E6 synthetic peptides: identification of T cell determinants, HLA-DR restriction and virus type specificity
AUTHOR(S): Strang, George; Hickling, Julian K.; McIndoe, G. Angus J.; Howland, Kevin; Wilkinson, David; Ikeda, Hitoshi; Rothbard, Jonathan B.
CORPORATE SOURCE: Lab. Mol. Immunol., Imp. Cancer Res. Fund, London, WC2A 3PX, UK
SOURCE: J. Gen. Virol. (1990), 71(2), 423-31
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Four T cell determinants in the major capsid protein of human **papillomavirus** (**HPV**) type 16 L1 and one in the **E6 protein** assocd. with cellular transformation were defined using synthetic peptides to stimulate peripheral blood mononuclear cells from asymptomatic individuals. HLA-DR restriction was defined using murine L cells transfected with HLA-DR genes to present antigen. Responses to two of the five determinants by T cell lines and clones were shown to be specific for **HPV**-16 based on the lack of cross-recognition of the corresponding sequences of other known **papillomavirus** sequences (types 1a, 5, 6b, 8, 11, 18, and 33). The T cells raised against two of the other peptides cross-reacted with corresponding peptides from other strains to varying extents, depending on their structural homol. The implications of these results regarding the prevalence of **HPV**-16 infection in the population and the possible diagnostic role of these responses in **papillomavirus** infection is discussed.

L20 ANSWER 43 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:421292 HCAPLUS
DOCUMENT NUMBER: 109:21292
TITLE: Identification of immunoreactive antigens of human

papillomavirus type 6b by using Escherichia coli-expressed fusion proteins

AUTHOR(S): Jenison, Steven A.; Firzlaff, Juliane M.; Langenberg, Andria; Galloway, Denise A.

CORPORATE SOURCE: Fred Hutchinson Cancer Res. Cent., Seattle, WA, 98104, USA

SOURCE: J. Virol. (1988), 62(6), 2115-23
CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human **papillomaviruses** (**HPVs**) infect the genital epithelium and are found in proliferative lesions ranging from benign condylomata to invasive carcinomas. The immunol. response to these infections is poorly understood because of the lack of purified viral antigens. In this study, bacterially derived fusion proteins expressing segments of all the major open reading frames (ORFs) of **HPV** type 6b (**HPV**-6b) were used in Western blot (immunoblot) assays to detect antibodies directed against **HPV**-encoded proteins. The most striking reactivities present in sera from patients with genital warts were to the **HPV**-6b **L1** ORF **protein** and, to a lesser extent, to the **HPV**-6b L2 ORF protein. Two cases of reactivity to **HPV**-6b E2 ORF were obsd., but no reactivities were seen with other **HPV**-6b constructs. Two sera reacted with the **HPV**-16 L2 fusion protein, and 2 sera reacted with the **HPV** -16 **E4 protein**. The antibodies directed against the **HPV**-6b fusion proteins showed no cross-reactivity with comparable regions of the **HPV**-16 ORFs. This assay provides a useful approach for further studies of **HPV** serol.

L20 ANSWER 44 OF 46 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1987:453075 HCAPLUS

DOCUMENT NUMBER: 107:53075

TITLE: Nucleotide sequence and comparative analysis of the human **papillomavirus** type 18 genome. Phylogeny of **papillomaviruses** and repeated structure of the E6 and E7 gene products

AUTHOR(S): Cole, S. T.; Danos, O.

CORPORATE SOURCE: Unite Appl. Genie Genet., Inst. Pasteur, Paris, 75724, Fr.

SOURCE: J. Mol. Biol. (1987), 193(4), 599-608
CODEN: JMOBAK; ISSN: 0022-2836

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The complete nucleotide sequence and genomic organization of human **papillomavirus** type 18, assocd. with cervical cancer, was established. A detailed comparative anal. was undertaken, leading to the identification of a no. of features specific for genital **papillomaviruses** and the construction of a phylogenetic tree. Genital **papillomaviruses** differ from other human and animal **papillomaviruses**, as they possess a longer E1 open reading frame (ORF) and have a characteristic control region. Phylogenetically, **HPV** 18 is located between the benign genital viruses, **HPV** 6 and **HPV** 11, and the malignant isolates, **HPV** 16 and **HPV** 33, and may represent an evolutionary intermediate among oncogenic **papillomaviruses**. Viral gene products known to be involved in cellular transformation are those of ORFs E5, E6, and E7.

Significant sequence variation was found between the E6 to E7 regions of different integrated forms of **HPV** 18. On re-examn. of the E6 primary structures, it was noticed that the gene has evolved by successive duplications of a unit encoding 33 amino acids, which include a Cys-X-X-Cys motif. Furthermore, the E7 gene product has apparently evolved in the same manner and is related to E6. Both gene products bear a striking resemblance to the transcriptional factor IIIA of Xenopus laevis, the prototype of a new class of nucleic acid-binding proteins.

IT **109300-89-2 109300-90-5 109300-91-6**
109300-92-7 109300-93-8
RL: PRP (Properties)
(amino acid sequence of)

IT **109300-76-7 109300-77-8 109300-78-9**
109300-79-0 109300-80-3 109300-81-4
109300-82-5 109300-83-6
RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence of)

L20 ANSWER 45 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1984:115638 HCAPLUS
DOCUMENT NUMBER: 100:115638
TITLE: DNA sequence and genome organization of genital human **papillomavirus** type 6b
AUTHOR(S): Schwarz, E.; Duerst, M.; Demankowski, C.; Lattermann, O.; Zech, R.; Wolfsperger, E.; Suhai, S.; Zur Hausen, H.
CORPORATE SOURCE: Inst. Virol., Univ. Freiburg, Freiburg, 7800, Fed. Rep. Ger.
SOURCE: EMBO J. (1983), 2(12), 2341-8
CODEN: EMJODG; ISSN: 0261-4189
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The complete nucleotide sequence of the circular double-stranded DNA of the genital human **papillomavirus** type 6b (**HPV6b**), comprising 7902 base pairs, was detd. and compared with the DNA sequences of human **papillomavirus** type 1a (**HPV1a**) and bovine **papillomavirus** type 1 (BPV1). All major open reading frames are located on 1 DNA strand only. Their arrangement reveals that the genomic organization of **HPV6b** is similar to that of **HPV1a** and BPV1. The putative early region includes 2 large open reading frames, E1 and E2, with marked amino acid sequence homologies to **HPV1a** and BPV1, which are flanked by several smaller frames. The internal part of E2 completely overlaps with another open reading frame, E4. The putative late region contains 2 large open reading frames L1 and L2. The L1 amino acid sequences are highly conserved among examd. **papillomavirus** types. By sequence comparison, potential promoter, splicing, and polyadenylation signals can be localized in **HPV6b** DNA; possible mechanisms of genital **papillomavirus** gene expression are suggested.

L20 ANSWER 46 OF 46 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1983:433750 HCAPLUS
DOCUMENT NUMBER: 99:33750
TITLE: Comparative analysis of the human type 1a and bovine type 1 **papillomavirus** genomes
AUTHOR(S): Danos, Olivier; Engel, Linda W.; Chen, Ellson Y.;

Yaniv, Moshe; Howley, Peter M.
CORPORATE SOURCE: Dep. Biol. Mol., Inst. Pasteur, Paris, 75724/15, Fr.
SOURCE: J. Virol. (1983), 46(2), 557-66
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The DNA sequences of the genomes of the bovine type 1 and human type 1a **papillomaviruses** were compared. The overall organization of both genomes is very similar. Three areas of maximal homol. were found in the L1 and E1/E2 genes, and at the beginning of L2. The conservation of homologous amino acid sequences encoded in the open reading frames argues that these segments represent real genes or exons. Within these segments, however, only certain domains of the putative proteins are preferentially conserved. Two polypeptide chains show homologous arrangement of the cysteine residue clusters Cys-X-X-Cys, despite a lack of conservation of the rest of the amino acid sequence. A significant sequence divergence in a region where the 3 reading frames are open suggests that **papillomavirus** genomes have evolved not solely by accumulation of point mutations. Conserved sequences were also found in the noncoding region; their possible involvement in regulation of viral gene expression is discussed.

=> d stat que

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L1          164 SEA FILE=REGISTRY HPV?
L2          872 SEA FILE=REGISTRY PROTEIN E?/CN
L3           74 SEA FILE=REGISTRY "PROTEIN L1"?/CN
L4       172330 SEA FILE=HCAPLUS L1 OR HPV? OR PAPILLOMA?
L5         1659 SEA FILE=HCAPLUS PROTEIN(W)E OR L2
L6          910 SEA FILE=HCAPLUS "PROTEIN L1"? OR L3
L8           19 SEA FILE=HCAPLUS L5 AND L6
L9            5 SEA FILE=HCAPLUS L4 AND L8
L10        2069 SEA FILE=HCAPLUS PROTEIN(W)E#
L11        2607 SEA FILE=HCAPLUS L2 OR L10
L12         885 SEA FILE=HCAPLUS PROTEIN(W)L1?
L13         910 SEA FILE=HCAPLUS L6 OR L12
L14          34 SEA FILE=HCAPLUS L11 AND L13
L15          19 SEA FILE=HCAPLUS L14 AND L4
L16          14 SEA FILE=HCAPLUS L15 NOT L9
L17        1700 SEA FILE=HCAPLUS L13 OR PROTEIN(2A)L1?
L18       16583 SEA FILE=HCAPLUS L11 OR PROTEIN(2A)E#
L19          65 SEA FILE=HCAPLUS L17 AND L18 AND L4
L20          46 SEA FILE=HCAPLUS L19 NOT (L9 OR L16)
L21        6038 SEA FILE=HCAPLUS L4 AND (?CANCER? OR ?CARCINO? OR ?MALIG? OR
                ?TUMOR? OR ?TUMOUR? OR ?NEOPLAS?)
L22        2052 SEA FILE=HCAPLUS L21 AND (LARYNX?  OR THROAT?  OR GENITAL? OR
                CERVI? OR PENIS OR VULVA OR ANUS?)
L23          69 SEA FILE=HCAPLUS L22 AND (CAPSID? OR CAPSOMER?)
L24          61 SEA FILE=HCAPLUS L23 NOT (L20 OR L9 OR L16)
L25          10 SEA FILE=HCAPLUS FUSION(2A)PROTEIN? AND L24
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=> d stat que l25 1-10

'1-10' IS NOT VALID HERE

For an explanation, enter "HELP DISPLAY QUERY".

=> d ibib abs hitrn l25 1-10

L25 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:158670 HCAPLUS
DOCUMENT NUMBER: 133:57189
TITLE: Human **papillomavirus** vaccines
AUTHOR(S): Breitburd, Francoise; Coursaget, Pierre
CORPORATE SOURCE: Unite des Papillomavirus, Unite Mixte Institut Pasteur/INSERM U190, Institut Pasteur, Paris, 75015, Fr.
SOURCE: Semin. Cancer Biol. (1999), 9(6), 431-444
CODEN: SECBE7; ISSN: 1044-579X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 99 refs. **Genital** human **papillomavirus** (**HPV**) infections are the viral sexually transmitted diseases most frequently diagnosed that include anogenital condylomas and squamous intra-bepithelial lesions, among which the precursors of invasive **carcinomas** of the uterine **cervix**. In animal PV models, vaccination against L1 and/or L2 viral **capsid** proteins provides an efficient protection against infection, involving virus type-specific neutralizing antibodies. Vaccination against non-structural E1, E2, E6 or E7 viral proteins does not prevent infection, unless administered altogether, but tends to stimulate regression, warranting the design of therapeutic vaccines. Prophylactic vaccines based on the use of virus-like particles (VLPs) obtained by auto-assembly of L1 or L1 and L2 proteins produced by recombinant DNA technol. are under phase I/II clin. trials for **HPV6**/11 assocd. with condylomas and for **HPV16** , the most frequent oncogenic genotype. Second generation vaccines are chimeric proteins or VLPs incorporating one of the structural proteins (L1 or L2) fused to a non-structural protein (E6, E7 or E2), which should induce both humoral and cellular immunity. Vaccine valency (no. of genotypes), route of administration (humoral vs. local immunity), vaccines (children, young adults, gender) and forms of vaccines (recombinant LSalmonella typhimurium*IL, edible plants expressing L1 and L2 proteins, DNA vaccines, synthetic antigenic peptides) are under study. End points to evaluate vaccine efficacy in phase III trials should include viral DNA detection and typing, and screening for low or high grade intraepithelial lesions. Therapeutic vaccines based on recombinant **HPV** E6 and/or E7 vaccinia virus, L2-E7 **fusion proteins** or E7 peptides corresponding to cytotoxic T cell epitopes are currently tested (phase I/II trials) in patients with **cervical carcinomas** of advanced clin. stages or high grade intraepithelial lesions. Animal studies, phase I/II clin. trials and implementation of the community support that **HPV** vaccines will constitute an efficient means to prevent **carcinoma** of the uterine **cervix**. (c) 1999 Academic Press.
REFERENCE COUNT: 97
REFERENCE(S): (2) Benyacoub, J; Infec Immun 1999, V67, P3674 HCAPLUS
(3) Bergquist, C; Infect Immun 1997, V65, P2676 HCAPLUS
(7) Boursnell, M; Vaccine 1996, V14, P1485 HCAPLUS

(10) Breitburd, F; J Virol 1995, V69, P3959 HCAPLUS
(12) Breitburd, F; Semin Cancer Biol 1996, V7, P359 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:626218 HCAPLUS
DOCUMENT NUMBER: 131:262610
TITLE: Formulation having a **papilloma** virus-specific protein
INVENTOR(S): Burger, Alexander; Gabelsberger, Josef
PATENT ASSIGNEE(S): Medigene Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948917	A2	19990930	WO 1999-EP1999	19990324
WO 9948917	A3	19991209		
W: AU, CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19812940	A1	19991007	DE 1998-19812940	19980324
AU 9935989	A1	19991018	AU 1999-35989	19990324
EP 1066321	A2	20010110	EP 1999-917850	19990324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: DE 1998-19812940 19980324
WO 1999-EP1999 19990324

AB **Papilloma** virus-specific early and late proteins are sol. in formulations contg. 0.3-.apprx.4M salt with pH 7.3-7.45. Formulations contg. these proteins, as well as deletion mutants and chimeric proteins which form viruslike particles, are useful for therapeutic and diagnostic purposes. Thus, a human **papilloma** virus 16 L1E7 **fusion protein** gene was constructed by recombinant DNA technol., and expressed as viruslike particles in Trichoplusia ni cells using a baculovirus vector.

L25 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:363228 HCAPLUS
DOCUMENT NUMBER: 127:93874
TITLE: Immunogenicity and reactogenicity of a recombinant **HPV6 fusion protein** vaccine adjuvanted with monophosphoryl lipid A
AUTHOR(S): Thompson, Stephen; Davies, Marie; O'Neill, Terry; Holding, Finn; Mann, Alison; Martin, Gilly; Varley, Clare; Watts, Maria; Beech, Jonathan; Thompson, Stephen J.; Leesman, Glen; Ulrich, Terry
CORPORATE SOURCE: Cantab Pharmaceuticals, Cambridge, CB4 4GN, UK
SOURCE: Biochem. Soc. Trans. (1997), 25(2), 274S
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A vaccine is being developed to stimulate the regression and prevent the recurrence of **genital** warts induced by infection with the human **papillomavirus** 6. This vaccine is a recombinant **fusion protein** of the L2 **capsid** protein and the E7 gene product (L2E7). Here, the authors studied the comparative immunogenicity and reactogenicity of the L2E7 **fusion protein** in either Alhydrogel, oil-in-water microemulsions, or aq. adjuvant formulations contg. monophosphoryl lipid A (MPL). The results indicate that the simple addn. of MPL to L2E7 already adsorbed onto Alhydrogel preferentially enhances in vitro interferon .gamma. formation and T cell proliferative responses in mice without increasing its reactogenicity in rabbits. To stimulate max. T cell response with L2E7 adjuvanted with Alhydrogel and MPL the rel. concns. of all components need to be optimized.

L25 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:733934 HCAPLUS
DOCUMENT NUMBER: 126:2474
TITLE: Synthetic human **papillomavirus** 6a and 11 major **capsid** protein L1 chimeric gene expression in Saccharomyces cerevisiae and use in vaccine development
INVENTOR(S): Hofmann, Kathryn J.; Jansen, Kathrin U.; Neeper, Michael P.; Joyce, Joseph G.; George, Hugh A.; Lehman, E. Dale
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630520	A2	19961003	WO 1996-US4117	19960325
WO 9630520	A3	19961107		
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, US, UZ, VN, AM, AZ, BY, KG, KZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9655277	A1	19961016	AU 1996-55277	19960325
AU 708111	B2	19990729		
CA 2216827	AA	19961003	CA 1996-2216827	19960326
EP 817852	A2	19980114	EP 1996-912467	19960326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1185810	A	19980624	CN 1996-194196	19960326
JP 11503313	T2	19990326	JP 1996-529596	19960326
ZA 9602526	A	19960904	ZA 1996-2526	19960329
NO 9704514	A	19971127	NO 1997-4514	19970929
US 6159729	A	20001212	US 1998-913462	19980126
PRIORITY APPLN. INFO.:			US 1995-413571	19950330

US 1995-413572 19950330
WO 1996-US4117 19960325

AB The present invention is directed to a chimeric gene encoding human **papillomavirus** type 6a L1 **protein fusion** products with human **papillomavirus** type 11 L1 protein. The chimeric gene is expressed using Saccharomyces cerevisiae fermn. The **fusion protein** has immunogenic properties useful for vaccine development and treatment of benign **genital** warts.

L25 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:207508 HCAPLUS
DOCUMENT NUMBER: 124:257934
TITLE: Proliferative T cell responses to human **papillomavirus** type 16 L1 peptides in patients with **cervical** dysplasia
AUTHOR(S): Shepherd, Philip S.; Rowe, Andrea J.; Cridland, Jeremy C.; Coletart, Timothy; Wilson, Philip; Luxton, Jenny C.
CORPORATE SOURCE: Dep. Immunology, Guy's Hospital Med. School, London, SE1 9RT, UK
SOURCE: J. Gen. Virol. (1996), 77(4), 593-602
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human **papillomavirus** type 16 (**HPV**-16) can cause **genital** warts, **cervical** dysplasias, and **carcinoma** of the **cervix**. Cell-mediated immunity is thought to be important in protection against the virus and in its elimination, but little is known about the mechanisms involved. In a cross-sectional study the authors demonstrated proliferative T cell responses to peptides representing the **HPV**-16 L1 **capsid** protein (aa 199-409) in the peripheral blood of 63% of patients with histol. evidence of **cervical** dysplasia and in 45% of healthy age-matched controls. This was achieved by generating short-term T cell lines (STLs) from each individual in vitro against a .beta.-galactosidase-**HPV**-16 L1 (aa 199-409) **fusion protein** for 2 wk, and then identifying the **HPV** epitopes they recognized with overlapping synthetic peptides (15-mers) spanning this region in 3 day specificity assays. Histol. grading and **HPV** typing by PCR were performed on patients' **cervical** biopsies taken at the same clin. visit as the peripheral blood samples. An immunogenic region was identified between aa 311-345 in 73% of patients (18% in controls) who responded to **HPV**-16 L1 (aa 199-409). The no. of responders to this region was higher in patients with **HPV**-16-pos. biopsies when compared to those with **HPV**-16-neg. biopsies, as was the no. of responders to individual peptides 311-325 (NLASSNYFPTPSGSM) and 321-335 (PSGSMVTSDAQIFNK) representing this region. The mean level of response to each individual peptide was also higher in the patient group than the controls. The most significant finding was that all patients with evidence of a current **HPV**-16 infection responded to .gtoreq.1 L1 peptides and 92% had high grade **cervical** intraepithelial **neoplasia** (CIN III). The authors also found that the CIN III group was more likely to respond to any L1 peptide than either the atypical group or the controls. Data from 4 individuals showed that the majority of peptide-specific STLs were CD4+ but some CD8+ STLs were also detected.

L25 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:256296 HCAPLUS
DOCUMENT NUMBER: 122:29196
TITLE: Analysis of type-restricted and cross-reactive epitopes on virus-like particles of human **papillomavirus** type 33 and in infected tissues using monoclonal antibodies to the major **capsid** protein
AUTHOR(S): Sapp, Martin; Kraus, Ute; Volpers, Christoph; Snijders, Peter J. F.; Walboomers, Jan M. M.; Streeck, Rolf E.
CORPORATE SOURCE: Inst. Med. Mikrobiologie, Johannes-Gutenberg-Univ. Mainz, Mainz, D-55101, Germany
SOURCE: J. Gen. Virol. (1994), 75(12), 3375-83
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A panel of six monoclonal antibodies recognizing at least three different antigenic regions has been raised against the L1 major **capsid** protein of human **papillomavirus** type 33 (**HPV**-33), which is assocd. with **cervical carcinoma**. The antigenic sites defined by these antibodies have been mapped and classified as type-restricted or broadly cross-reactive using bacterially expressed LI **fusion proteins** of a variety of **HPV** types. Conformational and linear epitopes have been distinguished using native and denatured virus-like particles. **HPV** infection of **genital** lesions has been analyzed using both monoclonal antibodies and DNA amplification by PCR. The antibodies obtained should be useful to probe the structure of **HPV** **capsids** and to develop a general assay for the detection and classification of productive **HPV** infections.

L25 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:424011 HCAPLUS
DOCUMENT NUMBER: 119:24011
TITLE: Development of type-specific and cross-reactive serological probes for the minor **capsid** protein of human **papillomavirus** type 33
AUTHOR(S): Volpers, Christoph; Sapp, Martin; Komly, Carol A.; Richalet-Secordel, Pascale; Streeck, Rolf E.
CORPORATE SOURCE: Inst. Med. Mikrobiol., Univ. Mainz, Mainz, D-6500, Germany
SOURCE: J. Virol. (1993), 67(4), 1927-35
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human **papillomavirus** type 33 (**HPV33**) is assocd. with **malignant tumors** of the **cervix**. In an attempt to develop immunol. probes for **HPV33** infections, antisera against various bacterial **fusion proteins** carrying sequences of the minor **capsid** protein encoded by L2 were raised in animals. Antigenic determinants on the **HPV33** L2 protein were identified by using truncated **fusion proteins** and were classified as type-specific or cross-reactive with respect to **HPV1** , -8, -11, -16, and -18. Cross-reactive epitopes map to amino acids 98 to

107 or to amino acids 102 to 112 and 107 to 117, resp., depending on the **fusion protein** used for immunization. Antibodies directed toward these epitopes detect L2 proteins of **HPV11**, -16, and -18, but not of **HPV1** and -8, in Western immunoblots and ELISAs. **HPV33** L2 amino acids 82 to 94 and 117 to 130 induce type-specific antibodies, with the major response directed to amino acids 117 to 130. By using a synthetic peptide corresponding to L2 amino acids 117 to 130, high-titered, type-specific antisera were obtained. These antisera should be useful as immunol. probes for **HPV33** infection.

L25 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:421849 HCAPLUS
DOCUMENT NUMBER: 113:21849
TITLE: An antigen chimera of poliovirus induces antibodies against human **papillomavirus** type 16
AUTHOR(S): Jenkins, Owen; Cason, John; Burke, Karen L.; Lunney, Declan; Gillen, Alison; Patel, Daksha; McCance, Dennis J.; Almond, Jeffrey W.
CORPORATE SOURCE: Dep. Microbiol., Univ. Reading, Reading, SE1 7EH, UK
SOURCE: J. Virol. (1990), 64(3), 1201-6
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has been established that the surface of poliovirus type 1 can be extensively modified to incorporate antigenic domains from other poliovirus serotypes and from unrelated viruses. The fact that the modified (chimeric) viruses exhibit dual antigenicity and immunogenicity led to exploring the possibility of using the Sabin vaccine strain of poliovirus type 1 as a vector for the presentation of antigenic domains from human **papillomavirus** type 16 (**HPV**-16), a virus assocd. with the development of **cervical carcinoma**. This report describes the construction and characterization of a chimeric poliovirus contg. a 16-residue sequence derived from the major **capsid** protein (L1) of **HPV**-16. This virus chimera stimulated the prodn. in rabbits of antibodies which recognized the **HPV**-16-derived peptide and an L1 **fusion protein** synthesized in Escherichia coli and detected **HPV**-16 in human biopsy material by immunoperoxidase staining. The possibility that poliovirus-**HPV** chimeras could be used as vaccines against **HPV**-16 is discussed.

L25 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:93221 HCAPLUS
DOCUMENT NUMBER: 110:93221
TITLE: Reactivities of polyclonal and monoclonal antibodies raised to the major **capsid** protein of human **papillomavirus** type 16
AUTHOR(S): Patel, Daksha; Shepherd, Philip S.; Naylor, Jennifer A.; McCance, Dennis J.
CORPORATE SOURCE: United Med. Dent. Sch., Guy's Hosp., London, SE1 9RT, UK
SOURCE: J. Gen. Virol. (1989), 70(1), 69-77
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polyclonal and monoclonal antibodies were raised against a **fusion protein** contg. .beta.-galactosidase and part of the major **capsid** protein L1 of the human **papillomavirus** (**HPV**) type 16. The polyclonal antibodies cross-reacted with the L1 protein of several **HPV** types including **HPV**-1, -2, -6 and -11 when reacted with virus-infected tissue sections, and with **HPV**-6 and -18 L1 **fusion proteins** on Western blotting. Monoclonal antibodies against the L1 **fusion protein** of **HPV**-16 reacted only with **HPV**-16 L1 **fusion proteins** on Western blots and with **HPV** -16-contg. biopsy sections as assessed by in situ DNA-DNA hybridization. These antibodies did not detect **HPV**-6 L1 protein after Western blotting or in **HPV**-6-infected tissue sections, although one did react with an **HPV**-18 **fusion protein** after Western blotting. The monoclonal antibodies were able to detect **HPV**-16 antigens in routine formaldehyde-fixed, wax-embedded sections of **cervical** intraepithelial **neoplasm** sections. **HPV**-16 L1 proteins were seen in one-third of biopsies that were pos. using the polyclonal cross-reacting antisera. Polyclonal antibodies to **fusion proteins** contg. part of the minor **capsid** protein L2 of **HPV**-6 or -16 appeared to be more type-specific as no cross-reactivity was seen when these antibodies were reacted with **HPV**-1- and -2-infected tissue sections.

L25 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:490524 HCAPLUS
DOCUMENT NUMBER: 109:90524
TITLE: Detection of human **papillomavirus** **capsid** antigens in various squamous epithelial lesions using antibodies directed against the L1 and L2 open reading frames
AUTHOR(S): Firzlaff, Juliane M.; Kiviat, Nancy B.; Beckmann, Anna Marie; Jenison, Steven A.; Galloway, Denise A.
CORPORATE SOURCE: Fred Hutchinson Cancer Res. Cent., Seattle, WA, 98104, USA
SOURCE: Virology (1988), 164(2), 467-77
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **HPV6** and **HPV16** infect the squamous epithelium of the **genital** tract and are thought to be involved in the pathogenesis of benign and **malignant** lesions. **HPV6** is primarily found in benign condylomas whereas **HPV16** is present in dysplasias and in invasive squamous cell **carcinomas**. To examine the expression of the major and minor **capsid** proteins in these lesions, polyclonal antisera directed against bacterially derived **fusion proteins** harboring different restriction fragments of the L1 and L2 ORFs of **HPV6b** and **HPV16** were generated. L1 ORF-specific antisera were not type-specific and detected the major **capsid** antigen in lesions infected with related **HPV** types. Anti-L2 ORF antisera could distinguish among **HPV1**, **HPV6**, and **HPV16** when the **fusion protein** used as the immunogen did not harbor the amino-terminus of the L2 ORF. The anti-L1 ORF antisera were employed to detect the major **capsid** protein in various lesions by immunohistochem. staining. Lesions harboring **HPV16** were pos. in a high percentage of

cervical intraepithelial **neoplasia** I-II (87%), and less frequently in **carcinomas** in situ (29%) or invasive **carcinomas** (17%). In all cases **capsid** antigen expression was restricted to cells showing some differentiation at the surface or periphery of the lesion.

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ds

Set .   Items   Description
S1        117   (PAPILLOMA?  OR HPV?) AND  PROTEIN(2N)E? ? AND PROTEIN(2N)
            L1?
S2         96   RD (unique items)
S3         47   S2 AND (CANCER? OR CARCINO? OR MALIG? OR TUMOR? OR TUMOUR?
            OR NEOPLAS?)
?show files
File 155:MEDLINE(R) 1966-2000/Dec W4
         (c) format only 2000 Dialog Corporation
File   5:Biosis Previews(R) 1969-2001/Mar W1
         (c) 2001 BIOSIS
File  34:SciSearch(R) Cited Ref Sci 1990-2001/Mar W2
         (c) 2001 Inst for Sci Info
File  35:Dissertation Abstracts Online 1861-2001/Feb
         (c) 2001 UMI
File  71:ELSEVIER BIOBASE 1994-2001/Mar W2
         (c) 2001  Elsevier Science B.V.
File  73:EMBASE 1974-2001/Mar W1
         (c) 2001 Elsevier Science B.V.
File  76:Life Sciences Collection 1982-2001/Dec
         (c) 2001 Cambridge Sci Abs
File 144:Pascal 1973-2001/Mar W1
         (c) 2001 INIST/CNRS
File 149:TGG Health&Wellness DB(SM) 1976-2001/Feb W4
         (c) 2001 The Gale Group
File 162:CAB HEALTH 1983-2001/Jan
         (c) 2001 CAB INTERNATIONAL
File 351:Derwent WPI 1963-2001/UD,UM &UP=200113
         (c) 2001 Derwent Info Ltd
File 357:Derwent Biotechnology Abs 1982-2001/Mar B2
         (c) 2001 Derwent Publ Ltd
File 440:Current Contents Search(R) 1990-2001/Mar W3
         (c) 2001 Inst for Sci Info
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Set     Items   Description
S1        117   (PAPILLOMA?  OR HPV?) AND  PROTEIN(2N)E? ? AND PROTEIN(2N)
            L1?
S2         96   RD (unique items)
S3         47   S2 AND (CANCER? OR CARCINO? OR MALIG? OR TUMOR? OR TUMOUR?
            OR NEOPLAS?)
?t s3/3 ab/1-47

 3/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.

07633646   93329139
   Relation  between  skin  cancer ,  humoral  responses  to  human
 papillomaviruses ,  and  HLA  class  II  molecules  in  renal  transplant
recipients.
  Bavinck JN;  Gissmann  L;  Claas  FH;  Van der Woude FJ; Persijn GG; Ter
Schegget J; Vermeer BJ; Jochmus I; Muller M; Steger G; et al
  Department of Dermatology, University Hospital, Leiden, The Netherlands.
  Journal of immunology (UNITED STATES)   Aug 1 1993,  151 (3) p1579-86,
ISSN 0022-1767   Journal Code: IFB
  Languages: ENGLISH
  Document type: JOURNAL ARTICLE
  Human  papillomaviruses   ( HPV  ),  especially  the  epidermodysplasia
```

verruciformis (EV)-associated HPV 5, 8, 14, 17, 20, and 47, are thought to play a role in the pathogenesis of some skin cancers in recipients of renal allografts. MHC class I and class II genes are involved in the cellular immune response to viral and tumor Ag. Little is known about humoral responses to HPV in recipients with and without skin cancer . We investigated the prevalence of antibodies to the early (E) protein E7 and the major capsid late (L) protein L1 of HPV 8. In addition, we studied the association of HLA class II molecules with these antibody responses. The E7 and L1 open reading frames of HPV 8 were bacterially expressed as beta-galactosidase fusion proteins, which were purified by preparative gel electrophoresis. Serum samples from 36 renal transplant recipients with and 91 recipients without skin cancer were screened for the presence of IgG and IgM antibodies to HPV 8 E7 and L1, by Western blot analysis. The detection of anti-HPV 8 L1 antibodies represents the immune response to HPV 8 and possibly other EV-associated HPV , because cross-reactivity between the representatives of this HPV subgenus can occur. The antibody responses to HLA Ag were used as controls. Recipients who had IgM antibodies but no IgG antibodies to L1 of HPV 8 (patients with no apparent class switch from IgM to IgG) had skin cancer in 50% of cases, whereas recipients who produced IgG antibodies (patients with an apparently good humoral response to L1 of HPV 8) had skin cancer in only 18% of cases. The estimated relative risk of skin cancer in recipients with no class switch, compared with the risk in those with a good humoral response, was 4.5 (95% confidence interval, 1.1 to 18.1). We found no association between the antibody response to HLA Ag and the occurrence of skin cancer . A strong linkage between the absent class switch of antibody production in response to L1 of HPV 8 and HLA-DR7 was observed (relative risk, 26.2). Renal transplant recipients who have no apparent class switch from IgM to IgG production in response to Ag encoded by L1 of HPV 8 or possibly other EV-associated HPV are at an increased risk of skin cancer . The association with HLA-DR7 indicates a genetic control of skin cancer development or regression, involving genes in the class II region of the MHC.

3/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06037578 86246690
Immunization against bovine papillomavirus infection.
Pilacinski WP; Glassman DL; Glassman KF; Reed DE; Lum MA; Marshall RF; Muscoplat CC; Faras AJ
Ciba Foundation symposium (NETHERLANDS) 1986, 120 p136-56, ISSN 0300-5208 Journal Code: D7X
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The two large open reading frames denoted L1 and L2 in the non-transforming region of the bovine papillomavirus type 1 (BPV-1) genome have been molecularly cloned to expression in Escherichia coli. Antisera against the E. coli-derived L1 and L2 protein reacted with BPV-1 in both enzyme-linked immunosorbent assays and immunoprecipitation reactions. Neutralization of BPV-induced transformation of mouse C127 cells was demonstrated most consistently with antisera against the L1 protein . E . coli-derived L1 protein protected calves against BPV-1 challenge after vaccination.

3/AB/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08938154 BIOSIS NO.: 199396089655
Relation between skin cancer, humoral responses to human papillomaviruses, and HLA class II molecules in renal transplant recipients.
AUTHOR: Bouwes-Bavinck Jan N(a); Gissmann Lutz; Claas Frans H J; Van Der Woude Fokko J; Persijn Guido G; Ter Schegget Jan; Vermeer Bert J; Jochmus Ingrid; Mueller Martin; et al
AUTHOR ADDRESS: (a)Dep. Dermatol., Univ. Hosp. Leiden, Rijnsburgerweg 10, 2333 AA Leiden**Netherlands Antilles
JOURNAL: Journal of Immunology 151 (3):p1579-1586 1993
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Human papillomaviruses (HPV), especially the epidermodysplasia verruciformis (EV)-associated HPV 5, 8, 14, 1 7, 20, and 47, are thought to play a role in the pathogenesis of some skin cancers in recipients of renal allografts. MHC class I and class II genes are involved in the cellular immune response to viral and tumor Ag. Little is known about humoral responses to HPV in recipients with and without skin cancer . We investigated the prevalence of antibodies to the early (E) protein E7 and the major capsid late (L) protein L1 of HPV 8. In addition, we studied the association of HLA class II molecules with these antibody responses. The E7 and L1 open reading frames of HPV 8 were bacterially expressed as beta-galactosidase fusion proteins, which were purified by preparative gel electrophoresis. Serum samples from 36 renal transplant recipients with and 91 recipients without skin cancer were screened for the presence of IgG and IgM antibodies to HPV 8 E7 and L1, by Western blot analysis. The detection of anti-HPV 8 L1 antibodies represents the immune response to HPV 8 and possibly other EV-associated HPV , because cross-reactivity between the representatives of this HPV subgenus can occur. The antibody responses to HLA Ag were used as controls. Recipients who had IgM antibodies but no IgG antibodies to L1 of HPV 8 (patients with no apparent class switch from IgM to IgG) had skin cancer in 50% of cases, whereas recipients who produced IgG antibodies (patients with an apparently good humoral response to L1 of HPV 8) had skin cancer in only 18% of cases. The estimated relative risk of skin cancer in recipients with no class switch, compared with the risk in those with a good humoral response, was 4.5 (95% confidence interval, 1.1 to 18.1). We found no association between the antibody response to HLA Ag and the occurrence of skin cancer . A strong linkage between the absent class switch of antibody production in response to L1 of HPV 8 and HLA-DR7 was observed (relative risk, 26.2). Renal transplant recipients who have no apparent class switch from IgM to IgG production in response to Ag encoded by L1 of HPV 8 or possibly other EV-associated HPV are at an increased risk of skin cancer . The association with HLA-DR7 indicates a genetic control of skin cancer development or regression, involving genes in the class II region of the MHC.

1993

3/AB/4 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abstracts Online

1022859 AAD8819081
EXPRESSION AND CHARACTERIZATION OF THE HUMAN PAPILLOMAVIRUS TYPE 6B OPEN

READING FRAME PROTEINS
Author: LI, CHOU-CHI HUANG
Degree: PH.D.
Year: 1988
Corporate Source/Institution: THE JOHNS HOPKINS UNIVERSITY (0098)
Source: VOLUME 49/07-B OF DISSERTATION ABSTRACTS INTERNATIONAL. PAGE 2501. 225 PAGES

A chemically synthesized peptide corresponding to residues 482 to 495 of the L1 late open reading frame (ORF) of human papillomavirus (HPV) type 6b, and a bacterially expressed 54-kDa fusion protein representing 92% of the L1 ORF protein (residue 39 to 500) were synthesized. The antiserum raised against the L1 fusion protein identified authentic L1 ORF products in HPV -1-induced (58 kDa) and HPV -6/11-induced (56 kDa) papillomas . The viral L1 protein has a basic isoelectric point and is probably modified. The synthetic peptide antiserum recognized the 56- to 58-kDa protein in HPV -6-induced warts, but not in HPV -1- or HPV -11-infected specimens. In situ immunostaining of tissue sections of a condyloma showed that the L1 protein was present exclusively in the nuclei of the koilocytes in superficial epithelium. The detected molecular mass and the histological distribution of the L1 protein confirmed that the L1 ORF product is the major viral capsid protein which contains the genus-specific (common) antigens. Using the fusion protein as antigen in immunoassays, corresponding antibodies in human sera were detected.

A 27-kDa fusion protein representing $\sp{\sim}$60% of the early ORF E2 product of HPV -6b (residues 25-232 out of 368 amino acids) was synthesized and partially sequenced. This E2 protein specifically bound the endonuclease-restricted DNA fragment which contained the long control region of HPV -6b genome. The E2 antiserum identified, for the first time, a 50-kDa protein in a majority of condylomas, and cervical carcinoma -derived cell lines, such as ME180, MS751, C-4I and C-4II. The E2-positive specimens were associated with HPV -6, -11, -16, -18 or unidentified HPVs . An oligopeptide (E2C) corresponding to residues 286 to 304 of the E2 ORF of HPV -6 was chemically synthesized. In a number of condylomas and cell lines, the affinity-purified E2C antiserum reacted with a 37-kDa putative E2 protein .

A protein representing $\sp{\sim}$96% of the HPV -6b L2 ORF was synthesized and used to elicit antibodies. In immunoblot analysis, the L2-antiserum reacted with a $\sp{\sim}$68-kDa protein only in HPV -6, -11 infected condylomas. The observed size matched with the size (68-76 kDa) of the minor capsid proteins reported in the literature. The L2 ORF probably encodes a minor viral capsid protein which is less cross-reactive than the major capsid protein encoded by the L1 ORF.

3/AB/5 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

01394957 2000071091
Synthesis of viral DNA and late capsid protein L1 in parabasal spinous cell layers of naturally occurring benign warts infected with human papillomavirus type 1
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Journal: Virology, 268/2 (281-293), 2000, United States
PUBLICATION DATE: March 15, 2000
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ISSN: 0042-6822

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LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 47

We investigated human papillomavirus type 1 (HPV1)-specific transcription, viral DNA replication, and viral protein expression in naturally occurring benign tumors by in situ hybridization, 5-bromodeoxyuridine (BrdU) incorporation, and immunohistochemistry and obtained results different from other HPV -infected benign tumors characterized so far. Moderate amounts of transcripts with a putative coding potential for E6/E7, E1, and E2 were demonstrated from the first subrabasal cell layer throughout the stratum spinosum and granulosum. In addition very large amounts of E4 and L1 transcripts were present in the same epithelial layers. This finding was substantiated by the demonstration of L1 and E4 protein already in the bottom-most spinous cell layer. Furthermore massive amplification of the viral DNA as measured by BrdU incorporation and different methods of in situ hybridization took place in the lowest 5 to 10 suprabasal cell layers. These findings are in contrast to the assumption that late gene expression and viral DNA synthesis are restricted to the more differentiated cell layers of the epithelium and point to differences in the regulation of the vegetative life cycle between different papillomavirus types. (C) 2000 Academic Press.

3/AB/6 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10606082 EMBASE No: 2000071328
Specific serum IgG, IgM and IgA antibodies to human papillomavirus types 6, 11, 16, 18 and 31 virus-like particles in human immunodeficiency virus-seropositive women
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Journal of General Virology (J. GEN. VIROL.) (United Kingdom) 2000, 81/3 (701-708)
CODEN: JGVIA ISSN: 0022-1317
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 32

To evaluate the humoral immune response to human papillomavirus (HPV) in women infected with human immunodeficiency virus (HIV), serum samples of 83 HIV-positive individuals were analysed by ELISA for specific antibodies of the isotypes IgG, IgA and IgM recognizing HPV -6, -11, -16, -18 and -31 L1 virus-like particles (VLPs), Papillomavirus -related lesions were present in 30 of 83 HIV-positive women. Twenty-one women (25%) presented with high-/intermediate-grade anogenital squamous intraepithelial lesions. PCR analysis and sequencing for HPV typing was done from biopsy specimens of 18 women; PCR-positive results were obtained in 90% of cases. In addition, HPV DNA hybrid capture assays were performed from cervical swabs of 58 HIV-positive women, 53% of whom had a positive result for high-risk HPV . Overall, positive IgG reactivity to HPV -6/-11 and HPV -16/-18/-31 was seen in 19%/31% and 49%/30%/24% of HIV-positive women, respectively. HPV -seropositivity was even higher than in 48 HIV-negative cervical intraepithelial neoplasia /cancer patients with percentages as follows: 8%/2% and 31%/15%/15%. This difference was significant for HPV -16 (P = 0.046). IgA responses were comparable to IgG, IgM responses were

low. The extraordinarily high rate of antibodies to the capsid protein L1 of high-risk HPVs (HPV -16, -18 and/or -31) in 58% of HIV-positive women compared to 19% (P = 0.00001) of 102 healthy HIV-negative control women suggests a high lifetime cumulative exposure to HPV and increased expression of capsid proteins due to cellular immunodeficiency in HIV-infected women.

3/AB/7 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

07625943 EMBASE No: 1999112358
Induction of HPV16 capsid protein-specific human T cell responses by virus-like particles
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W.M. Kast, Cancer Immunology Program, Cardinal Bernardin Cancer Center, Loyola University of Chicago, 2160 S. First Avenue, Maywood, IL 60153 United States
Biological Chemistry (BIOL. CHEM.) (Germany) 1999, 380/3 (335-340)
CODEN: BICHF ISSN: 1431-6730
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 22

It has been postulated that upon binding to a cell surface receptor, papilloma virus-like particles (VLPs) gain entry into the cytosol of infected cells and the capsid proteins L1 and L2 can be processed in the MHC class I presentation pathway. Vaccination of mice with human papilloma virus-like particles consisting of capsid proteins L1 and L2 induced a CD8-mediated and perforin dependent protective immune response against a tumor challenge with human papilloma virus transformed tumor cells, which express only minute amounts of L1 protein . Here we show that HPV16 capsid proteins stimulate a MHC class I restricted CTL response with human peripheral blood lymphocytes (PBL) in vitro. The vigorous response was specific for VLP-infected target cells and was MHC class I restricted. Moreover we show the presence of at least one HLA-A*0201 restricted CTL epitope within the HPV -16 capsid proteins by using a VLP-'infected' HLA-A*0201 transfected human cell line as target cells. These results demonstrated that VLPs can induce a HPV16 capsid protein-specific immune response in humans, allowing the monitoring of immune responses induced by vaccines based on chimeric VLPs carrying additional immunogenic peptides or proteins in therapeutical applications in human patients.

3/AB/8 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

07615073 EMBASE No: 1999091645
Induction of autoantibodies to mouse CCR5 with recombinant papillomavirus particles
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Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 02 MAR 1999 , 96/5 (2373-2378)
CODEN: PNASA ISSN: 0027-8424

DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 37

The vertebrate immune system has evolved to respond vigorously to microbial infection but to ignore self-antigens. Evidence has emerged that B cell responses to viruses are initiated by immune recognition of ordered arrays of antigen on the viral surface. To test whether autoantibodies against a self-antigen can be induced by placing it in a context that mimics the ordered surface of a viral particle, a peptide representing an extracellular loop of the mouse chemokine receptor CCR5 was incorporated into an immunodominant site of the bovine papillomavirus virus L1 coat protein , which self-assembles into virus-like particles. Mice inoculated with chimeric L1-CCR5 particles generated autoantibodies that bound to native mouse CCR5, inhibited binding of its ligand RANTES, and blocked HIV-1 infection of an indicator cell line expressing a human-mouse CCR5 chimera. These results suggest a general method for inducing autoantibodies against self-antigens, with diverse potential basic research and clinical applications.

3/AB/9 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

07583693 EMBASE No: 1999074258
Immune responses against human papillomavirus (HPV) type 16 virus-like particles in a cohort study of women with cervical intraepithelial neoplasia. I. Differential T-helper and IgG responses in relation to HPV infection and disease outcome

De Gruijl T.D.; Bontkes H.J.; Walboomers J.M.M.; Coursaget P.; Stukart M.J.; Dupuy C.; Kueter E.; Verheijen R.H.M.; Helmerhorst T.J.M.; Duggan-Keen M.F.; Stern P.L.; Meijer C.J.L.M.; Scheper R.J.
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Journal of General Virology (J. GEN. VIROL.) (United Kingdom) 1999, 80/2 (399-408)
CODEN: JGVIA ISSN: 0022-1317
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 33

T-helper (Th) cell-dependent IL-2 production and plasma IgG responses to virus-like particles consisting of the human papillomavirus type 16 (HPV -16) major capsid protein L1 (L1 -VLP) were determined in patients with cytological evidence of cervical intraepithelial neoplasia (CIN) participating in a non-intervention prospective cohort study. IgG responses were associated with HPV -16 persistence and high-grade CIN lesions, while high frequencies of Th responses were observed in patients with both virus clearance and virus persistence, irrespective of CIN grade. The IgG response was found in conjunction with an IL-2 response to L1-VLP in 87% of the patients. Recognition of the HPV -16 L1 Th epitope (amino acids 311-335) was found to be more closely associated than recognition of L1-VLP as a whole to HPV exposure and CIN development. Among the HPV -16sup + patients included in this study, those showing a Th response to amino acids 311-335 were more likely to carry the HLA DRB1*11/DQB1*0301 haplotype, while those showing an IgG response to L1-VLP were more likely to carry DRB1*0101/DQB1*0501. However, neither cell-mediated nor humoral immune responses against HPV -16L1 appear to be sufficient for the natural control of HPV infection and CIN development.

3/AB/10 · (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

07356081 EMBASE No: 1998225574
Detection of human papillomavirus DNa in PUVA-associated non-melanoma skin cancers
Harwood C.A.; Spink P.J.; Surentheran T.; Leigh I.M.; Hawke J.L.M.; Proby C.M.; Breuer J.; McGregor J.M.
Dr. C.A. Harwood, Center for Cutaneous Research, Royal London Sch. of Med. and Dent., Queen Mary and Westfield College, 2 Newark Street, London E1 2AT United Kingdom
Journal of Investigative Dermatology (J. INVEST. DERMATOL.) (United States) 1998, 111/1 (123-127)
CODEN: JIDEA ISSN: 0022-202X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 40

Psoralen and UVA (PUVA) photochemotherapy is associated with a dose-dependent increased risk of nonmelanoma skin cancer in patients treated for psoriasis. Like ultraviolet B radiation, PUVA is both mutagenic and immunosuppressive and may thus act as a complete carcinogen ; however, the reversed squamous to basal cell carcinoma ratio (SCC:BCC) in PUVA-treated patients, also seen in immunosuppressed renal transplant recipients, suggests a possible cofactor role for human papillomavirus (HPV) infection. In this study we examine a large series of benign and malignant cutaneous lesions for the presence of HPV DNA from patients treated with high dose (<=500 J per cmsup 2) ultraviolet A. A panel of degenerate primers based on the L1 (major capsid protein) open reading frame was employed, designed to detect mucosal, cutaneous, and epidermodysplasia verruciformis HPV types with high sensitivity and specificity. HPV DNA was detected in 15 of 20 (75%) non- melanoma skin cancer , seven of 17 (41.2%) dysplastic PUVA keratoses, four of five (80%) skin warts, and four of 12 (33%) PUVA-exposed normal skin samples. The majority of HPV positive lesions contained epidermodysplasia verruciformis-related HPV including HPV -5, -20, -21, -23, -24, and -38. Possible novel epidermodysplasia verruciformis types were identified in further lesions. Mixed infection with epidermodysplasia verruciformis, cutaneous, and/or mucosal types was present in six of 30 (20%) of all HPV positive lesions, including in normal skin, warts, dysplastic PUVA keratoses, and squamous cell carcinomas . The prevalence and type of HPV infection in cutaneous lesions from PUVA-treated patients is similar to that previously reported in renal transplant-associated skin lesions, and suggests that the role of HPV in PUVA-associated carcinogenesis merits further study.

3/AB/11 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

07301259 EMBASE No: 1998211276
In vitro gene transfer using human papillomavirus-like particles
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P. Coursaget, Institut de Virologie de Tours, Fac. Sci. Pharm. 'Philippe Maupas', 31 avenue Monge, 37200 Tours France
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Nucleic Acids Research (NUCLEIC ACIDS RES.) (United Kingdom) 01 MAR 1998, 26/5 (1317-1323)

CODEN: NARHA ISSN: 0305-1048
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 45

Recombinant papillomavirus -like particles have recently been shown to be highly effective for the prevention of papillomavirus infections and associated tumors , and a virus-like particle-based vaccine against the most prevalent HPV causing genital infection in humans will be developed in the near future. Another use of these virus-like particles may lie in gene therapy and DNA immunization. We report here that human papillomavirus -like particles composed of the major capsid protein (L1) of HPV -16 are able to package unrelated plasmid DNA in vitro and then to deliver this foreign DNA to eukaryotic cells with the subsequent expression of the encoded gene. The results indicate higher gene transfer than with DNA alone or with liposome. Virus-like particles are a very promising vehicle for delivering genetic material into target cells. Moreover, the preparation of the gene transfer vehicle is relatively easy.

3/AB/12 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

07252785 EMBASE No: 1998073192
Chimeric papillomavirus virus-like particles elicit antitumor immunity against the e7 oncoprotein in an hpv16 tumor model
Greenstone H.L.; Nieland J.D.; De Visser K.E.; De Bruijn M.L.H.; Kirnbauer R.; Roden R.B.S.; Lowy D.R.; Kast W.M.; Schiller J.T.
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Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 17 FEB 1998 , 95/4 (1800-1805)
CODEN: PNASA ISSN: 0027-8424
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 45

Papillomavirus -like particles (VLPs) are a promising prophylactic vaccine candidate to prevent human papillomavirus (HPV) infections and associated epithelial neoplasia . However, they are unlikely to have therapeutic effects because the virion capsid proteins are not detected in the proliferating cells of the infected epithelia or in cervical carcinomas . To increase the number of viral antigen targets for cell-mediated immune responses in a VLP-based vaccine, we have generated stable chimeric VLPs consisting of the L1 major capsid protein plus the entire E7 (11 kDa) or E2 (43 kDa) nonstructural papillomavirus protein fused to the L2 minor capsid protein. The chimeric VLPs are indistinguishable from the parental VLPs in their morphology and in their ability to agglutinate erythrocytes and elicit high titers of neutralizing antibodies. Protection from tumor challenge was tested in C57BL/6 mice by using the tumor cell line TC-1, which expresses HPV16 E7, but not the virion structural proteins. Injection of HPV16 L1/L2- HPV16 E7 chimeric VLPs, but not HPV16 L1/L2 VLPs, protected the mice from tumor challenge, even in the absence of adjuvant. The chimeric VLPs also induced protection against tumor challenge in major histocompatibility class II-deficient mice, but not in betainf 2-microglobulin or perforin knockout mice implying that protection was mediated by class I-restricted cytotoxic

lymphocytes. These findings raise the possibility that VLPs may generally be efficient vehicles for generating cell-mediated immune responses and that, specifically, chimeric VLPs containing papillomavirus nonstructural proteins may increase the therapeutic potential of VLP-based prophylactic vaccines in humans.

3/AB/13 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

06690996 EMBASE No: 1996355930
Papillomavirus-like particles for serology and vaccine development
Kirnbauer R.
DIAID, Department of Dermatology, University of Vienna Medical School, AKH Wahringer Gurtel 18-20,A-1090 Vienna Austria
Intervirology (INTERVIROLOGY) (Switzerland) 1996, 39/1-2 (54-61)
CODEN: IVRYA ISSN: 0300-5526
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Genital infection with high-risk human papillomaviruses (HPV) has been etiologically linked with the development of cervical and other anogenital cancers . There is therefore a need for an effective HPV vaccine with the potential to significantly reduce the burden of more than half a million new cervical cancer cases in women worldwide each year. The L1 major capsid protein of papillomaviruses expressed in eukaryotic cells self-assembles into virus-like particles (VLP). VLP are attractive subunit vaccine candidates since they lack potentially oncogenic papillomavirus DNA and express the conformationally dependent epitopes necessary to induce high-titer neutralizing antibodies, Prophylactic VLP vaccination has achieved a high degree of protection in animal studies. Thus VLP are now considered the immunogen of choice for human vaccine trials to prevent genital HPV infection. VLP of different HPV have been developed to study the serologic relationship between HPV types. VLP-based ELISA are able to detect antibodies in human sera and are now widely used in epidemiologic studies of the natural history of HPV infection and the associated risk of developing neoplasia .

3/AB/14 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

06462543 EMBASE No: 1996128485
Proliferative T cell responses to human papillomavirus type 16 L1 peptides in patients with cervical dysplasia
Shepherd P.S.; Rowe A.J.; Cridland J.C.; Coletart T.; Wilson P.; Luxton J.C.
Department of Immunology, Guy's Hospital Medical School, UMDS Guy's Hospital Trust, London Bridge,London SE1 9RT United Kingdom
Journal of General Virology (J. GEN. VIROL.) (United Kingdom) 1996, 77/4 (593-602)
CODEN: JGVIA ISSN: 0022-1317
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Human papillomavirus type 16 (HPV -16) can cause genital warts, cervical dysplasias and carcinoma of the cervix. Cell-mediated immunity is thought to be important in protection against the virus and in its elimination, but little is known about the mechanisms involved. In a

cross-sectional study we have demonstrated proliferative T cell responses to peptides representing the HPV -16 L1 capsid protein (aa 199-409) in the peripheral blood of 63% of patients (n = 41) with histological evidence of cervical dysplasia and in 45% of healthy age-matched controls (n = 11). This was achieved by generating short-term T cell lines (STLs) from each individual in vitro against a beta-galactosidase-HPV16 L1 (aa 199-409) fusion protein for 2 weeks, and then identifying the HPV epitopes they recognized with overlapping synthetic peptides (15-mers) spanning this region in 3 day specificity assays. Histological grading and HPV typing by PCR were performed on patients' cervical biopsies taken at the same clinical visit as the peripheral blood samples. An immunogenic region was identified between aa 311-345 in 73% of patients (18% in controls) who responded to HPV -16 L1 (aa 199-409). The number of responders to this region was significantly higher in patients with HPV -16-positive biopsies when compared to those with HPV -16-negative biopsies (P = 0.006), as was the number of responders to individual peptides 311-325 (NLASSNYFPTPSGSM; P = 0.04) and 321-335 (PSGSMVTSDAQIFNK; P = 0.004) representing this region. The mean level of response to each individual peptide was also higher in the patient group than the controls (P < 0.05). The most significant finding was that all patients with evidence of a current HPV -16 infection responded to one or more L1 peptides (P = 0.0004) and 92% had high grade cervical intraepithelial neoplasia (CIN III). We also found that the CIN III group was more likely to respond to any L1 peptide than either the atypical group (P = 0.04) or the controls (P = 0.05). Data from four individuals showed that the majority of peptide-specific STLs were CD4sup + but some CD8sup + STLs were also detected.

3/AB/15 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

06127464 EMBASE No: 1995158469
Immunization with viruslike particles from cottontail rabbit papillomavirus (CRPV) can protect against experimental CRPV infection
Breitburd F.; Kirnbauer R.; Hubbert N.L.; Nonnenmacher B.; Trin-Dinh-Desmarquet C.; Orth G.; Schiller J.T.; Lowy D.R.
Laboratory of Cellular Oncology, National Cancer Institute,Bethesda, MD 20892 United States
Journal of Virology (J. VIROL.) (United States) 1995, 69/6 (3959-3963)
CODEN: JOVIA ISSN: 0022-538X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We tested the ability of vaccination with virus-lib particles (VLPs) to protect domestic rabbits against papillomas induced by the cottontail rabbit papillomavirus (CRPV). A recombinant baculovirus system that expressed only the L1 major papillomavirus structural protein or L1 plus the minor L2 protein was used in insect cells as the source of VLPs. Groups of 10 rabbits were immunized with native or denatured VLPs from CRPV or type 1 bovine papillomavirus by using Freund's adjuvant. Alum was used as the adjuvant for an additional group immunized with CRPV L1-L2 VLPs. Animals were challenged with 5 x 10sup 1sup 0 and 2 x 10sup 1sup 1 particles on opposing flanks. No protection was seen in rabbits immunized with native or denatured bovine papillomavirus L1-L2 or with denatured CRPV L1-L2. In these groups, the lower and higher challenge doses resulted in 27 of 30 animals with extensive papillomas , with each of the remaining animals having a smaller number of persistent papillomas . Progression to carcinoma developed in 20 rabbits. Animals inoculated with native CRPV VLPs composed of L1 alone or L1-L2 developed many fewer lesions; the lower and higher challenge doses resulted in 17 of 29 and 5 of 29 rabbits,

respectively, with no lesions, and the remainder developed only one to eight papillomas , which all regressed except for those on 1 rabbit. None developed cancer within i year of infection. Rabbits vaccinated with native CRPV VLPs developed high-titer antibodies in an enzyme-linked immunosorbent assay based on native VLPs, and passive transfer of serum or immunoglobulin G from rabbits immunized with CRPV VLPs protected against CRPV challenge. We conclude that native VLPs can induce antibody-mediated, type- specific protection against experimental papillomavirus infection.

3/AB/16 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

05982239 EMBASE No: 1995009413
Analysis of type-restricted and cross-reactive epitopes on virus-like particles of human papillomavirus type 33 and in infected tissues using monoclonal antibodies to the major capsid protein
Sapp M.; Kraus U.; Volpers C.; Snijders P.J.F.; Walboomers J.M.M.; Streeck R.E.
Inst fur Medizinische Mikrobiologie, Johannes-Gutenberg-Universitat Mainz, Hochhaus am Augustusplatz,D-55101 Mainz Germany
Journal of General Virology (J. GEN. VIROL.) (United Kingdom) 1994, 75/12 (3375-3383)
CODEN: JGVIA ISSN: 0022-1317
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

A panel of six monoclonal antibodies recognizing at least three different antigenic regions has been raised against the L1 major capsid protein of human papillomavirus type 33 (HPV -33), which is associated with cervical carcinoma . The antigenic sites defined by these antibodies have been mapped and classified as type-restricted or broadly cross-reactive using bacterially expressed L1 fusion proteins of a variety of HPV types. Conformational and linear epitopes have been distinguished using native and denatured virus-like particles. HPV infection of genital lesions has been analysed using both monoclonal antibodies and DNA amplification by PCR. The antibodies obtained should be useful to probe the structure of HPV capsids and to develop a general assay for the detection and classification of productive HPV infections.

3/AB/17 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

05711484 EMBASE No: 1994127978
Sequence variation in the capsid protein genes of human papillomavirus type 16
Pushko P.; Sasagawa L.T.; Cuzick L.J.; Crawford L.
Imperial Cancer Research Fund, Department of Pathology, University of Cambridge,Cambridge CB2 1QP United Kingdom
Journal of General Virology (J. GEN. VIROL.) (United Kingdom) 1994, 75/4 (911-916)
CODEN: JGVIA ISSN: 0022-1317
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We have cloned and sequenced the L1 and L2 genes from human papillomavirus type 16 (HPV16) DNA-containing cervical cytology samples collected from the U.K. and Trinidad. Samples containing high copy numbers

of HPV16 DNA were selected as being likely to contain fully functional virus DNA molecules in an episomal state, rather than in an integrated and possibly altered state. In comparison with the previously published sequence of HPV16 isolated from an invasive cancer a variety of differences were detected in both L1 and L2. The pattern of changes appears to be different in samples from the two geographic regions. One of the differences (resulting in D at position 202 of the L1 protein) reported recently to be functionally important for virus particle assembly was found to occur in all the samples examined. Variations in L1 found within known immunoreactive regions or hydrophobic domains should be taken into account in design of prophylactic vaccines for HPV16 based on virus-like particles. All variations within L2 protein were found in hydrophilic domains in the carboxy-terminal half of L2. These positions were highly variable among other types of papillomavirus and are located outside the known L2 immunoreactive region.

3/AB/18 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

05412656 EMBASE No: 1993180755
Cottontail rabbit papillomavirus L1 protein-based vaccines: Protection is achieved only with a full-length, nondenatured product
Lin Y.-L.; Borenstein L.A.; Ahmed R.; Wettstein F.O.
Microbiology/Immunology Department, School of Medicine, University of California,Los Angeles, CA 90024-1747 United States
Journal of Virology (J. VIROL.) (United States) 1993, 67/7 (4154-4162)
CODEN: JOVIA ISSN: 0022-538X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Papillomas induced by the cottontail rabbit papillomavirus (CRPV) progress at a high frequency to carcinomas . In this regard, CRPV and its tumors can serve as an animal model for highly oncogenic human papillomaviruses . We have previously shown that immunization with major structural protein L1 elicits neutralizing antibodies and protects rabbits from papilloma development (Y.- L. Lin, L. A. Borenstein, R. Selvakumar, R. Ahmed, and F. O. Wettstein, Virology 187:612-619, 1992). In this study, we demonstrated that vaccination with the TrpE-L1 fusion protein not only protected rabbits from papilloma development but also prevented latent infection. This was indicated by the failure to amplify CRPV sequences by polymerase chain reaction in biopsies from infection sites of immunized animals. Furthermore, we showed that TrpE- L1 immunization protected rabbits from papilloma formation induced by virus but not from that induced by viral DNA. To explore the possibility of developing vaccines based on L1 subfragments, we mapped the linear L1 epitopes recognized by TrpE-L1-immunized rabbits and by virus-infected rabbits resistant to superinfection. Sera from papilloma -bearing rabbits reacted with one major epitope located at the carboxy-terminal end of L1, between amino acids (aa) 480 and 505. A second epitope, and in some animals a third one, was located in the amino-terminal region, between aa 78 and 101, as well as between aa 37 and 62. Sera from TrpE-L1-immunized animals recognized only one major epitope, located between aa 6 and 37. Immunization of rabbits with L1 subfragment fusion proteins led to seroconversion, but no neutralizing antibodies were produced and the animals were not protected against papilloma formation. The data indicate that a successful papillomavirus vaccine must be based on immunization with full-length native L1 and that further simplification to smaller peptides containing major linear epitopes is not feasible.

3/AB/19 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

05236724 EMBASE No: 1993004809
Papillomavirus L1 major capsid protein self-assembles into virus-like particles that are highly immunogenic
Kirnbauer R.; Booy F.; Cheng N.; Lowy D.R.; Schiller J.T.
Laboratory of Cellular Oncology, National Cancer Institute,Bethesda, MD 20892 United States
Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 1992, 89/24 (12180-12184)
CODEN: PNASA ISSN: 0027-8424
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Infection by certain human papillomavirus types is regarded as the major risk factor in the development of cervical cancer , one of the most common cancers of women worldwide. Analysis of the immunogenic and structural features of papillomavirus virions has been hampered by the inability to efficiently propagate the viruses in cultured cells. For instance, it has not been established whether the major capsid protein L1 alone is sufficient for virus particle assembly. In addition, it is not known whether L1, L2 (the minor capsid protein), or both present the immunodominant epitopes required for induction of high-titer neutralizing antibodies. We have expressed the L1 major capsid proteins of bovine papillomavirus type 1 and human papillomavirus type 16 in insect cells via a baculovirus vector and analyzed their conformation and immunogenicity. The L1 proteins were expressed at high levels and assembled into structures that closely resembled papillomavirus virions. The self-assembled bovine papillomavirus L1, in contrast to L1 extracted from recombinant bacteria or denatured virions, also mimicked intact bovine papillomavirus virions in being able to induce high-titer neutralizing rabbit antisera. These results indicate that L1 protein has the intrinsic capacity to assemble into empty capsid-like structures whose immunogenicity is similar to infectious virions. This type of L1 preparation might be considered as a candidate for a serological test to measure antibodies to conformational virion epitopes and for a vaccine to prevent papillomavirus infection.

3/AB/20 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE

04940017 EMBASE No: 1992080233
Detection of antibodies to a linear epitope on the major coat protein (L1) of human papillomavirus type-16 (HPV-16) in sera from patients with cervical intraepithelial neoplasia and children
Cason J.; Kambo P.K.; Best J.M.; McCance D.J.
Richard Dimbleby Laboratory, The Rayne Institute, St. Thomas's Hospital, Lambeth Palace Road,London SE1 7EH United Kingdom
International Journal of Cancer (INT. J. CANCER) (United States) 1992 , 50/3 (349-355)
CODEN: IJCNA ISSN: 0020-7136
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Antibodies to the major (LI) coat protein of human papilloma -virus type

16 (HPV -16) in sera from patients with cervical intra-epithelial neoplasia (CIN) have been investigated by means of recombinant proteins and synthetic peptides. When LI-HPV -16 fusion proteins were used in immunoblot assays, no antibody reactivity was found in sera from 52 patients with CIN or from 21 unrelated children. Amino-acid sequence analyses indicated that LI-HPV -16 amino acids 473 to 492 may contain an HPV -16 type-restricted epitope since the greatest diversity occurs in this region. In the ELISA, seropositivity to peptides 473 to 492 was more common among CIN patients whose biopsies contained HPV -16 DNA (91%, 21 of 23) than among their children (24%, 5 of 21;$p < 0.001$) or other CIN patients with HPV -16 DNA-negative biopsies (66%, 19 of 29; $p < 0.05$), but was unrelated to the severity of the CIN lesion. Antibodies to LI-HPV -16 peptide 473 to 492 among seropositive CIN patients cross-reacted with the analogous LI-HPV -33, but not with the LI-HPV -6b peptide, and were predominantly IgM. In contrast, antibodies which recognized a less variable region of LI-HPV -16 (amino acids 279 to 293) showed no association with HPV -16 DNA status. Seropositivity to the LI-HPV -6b (amino acids 473-492) was less frequent (33%) among CIN patients and unassociated with HPV -16 DNA status ($P > 0.01$); however 51% (37 of 72) of patients with genital warts had antibodies to this peptide.

3/AB/21 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

02480059 4700340
Human papillomavirus vaccines
Breitburd, F.; Coursaget, P.
Unite des Papillomavirus, Unite Mixte Institut Pasteur/INSERM U190,
Institut Pasteur, 25 rue du Docteur Roux, 75015 Paris, France
Seminars in Cancer Biology vol. 9, no. 6, pp. 431-445 (1999)
ISSN: 1044-579X
DOCUMENT TYPE: Journal article; Review article LANGUAGE: ENGLISH
SUBFILE: Virology & AIDS Abstracts; Oncogenes & Growth Factors Abstracts

Genital human papillomavirus (HPV) infections are the viral sexually transmitted diseases most frequently diagnosed that include anogenital condylomas and squamous intra-epithelial lesions, among which the precursors of invasive carcinomas of the uterine cervix. In animal PV models, vaccination against L1 and/or L2 viral capsid proteins provides an efficient protection against infection, involving virus type-specific neutralizing antibodies. Vaccination against non-structural E1, E2, E6 or E7 viral proteins does not prevent infection, unless administered altogether, but tends to stimulate regression, warranting the design of therapeutic vaccines. Prophylactic vaccines based on the use of virus-like particles (VLPs) obtained by auto-assembly of L1 or L1 and L2 proteins produced by recombinant DNA technology are under phase I/II clinical trials for HPV6 /11 associated with condylomas and for HPV16 , the most frequent oncogenic genotype. Second generation vaccines are chimeric proteins or VLPs incorporating one of the structural proteins (L1 or L2) fused to a non-structural protein (E6 , E7 or E2), which should induce both humoral and cellular immunity. Vaccine valency (number of genotypes), route of administration (humoral versus local immunity), vaccinees (children, young adults, gender) and forms of vaccines (recombinant Salmonella typhimurium, edible plants expressing L1 and L2 proteins, DNA vaccines, synthetic antigenic peptides) are under study. End points to evaluate vaccine efficacy in phase III trials should include viral DNA detection and typing, and screening for low or high grade intraepithelial lesions. Therapeutic vaccines based on recombinant HPV E6 and/or E7 vaccinia virus, L2-E7 fusion proteins or E7 peptides corresponding to cytotoxic T

cell epitopes are currently tested (phase I/II trials) in patients with cervical carcinomas of advanced clinical stages or high grade intraepithelial lesions. Animal studies, phase I/II clinical trials and implementation of the community support that HPV vaccines will constitute an efficient means to prevent carcinoma of the uterine cervix.

3/AB/22 (Item 2 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

02241044 4249847
p53 alterations and HPV infections are common in oral SCC: p53 gene mutations correlate with the absence of HPV 16-E6 DNA
Penhallow, J.; Steingrimsdottir, H.; Elamin, F.; Warnakulasuriya, S.; Farzaneh, F.; Johnson, N.; Tavassoli, M.
RCS Department of Dental Sciences, King's College School of Medicine and Dentistry, The Rayne Institute, 123 Coldharbour Lane, London SE5 9NU, UK
Int. J. Oncol. vol. 12, no. 1, pp. 59-68 (1998)
ISSN: 1019-6439
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Oncogenes & Growth Factors Abstracts; Virology & AIDS Abstracts

To examine the association between HPV infections and p53 gene aberrations, a panel of 28 oral squamous cell carcinomas (SCC) and 12 potentially malignant oral mucosal lesions were analysed for p53 mutations in exons 2-9. p53 protein was analysed by immunocytochemistry using DO7 antibody. The same panel was also examined for the possible presence of HPV infection. p53 overexpression was detected in 13/26 (50%) malignant and 2/9 (22%) premalignant lesions. Mutations in the coding region of the p53 gene were found in 10 malignant samples. None of the premalignant lesions were shown to have p53 mutations. The total number of p53 mutations in 10 samples were 14 of which 12 (85%) were in exon 5 suggesting the presence of hot spots in exon 5 for carcinogens involved in the transformation of oral epithelial cells. The presence of HPV DNA was first screened with consensus primers to the L1 region and nested PCR approach. HPV 6 and HPV 16 were detected in 14/28 (50%) oral SCC and 4 of 12 (33%) precancerous lesions, 7 tumours harboured both types. The samples were then examined for the presence of E6 oncogenic sequence of HPV16 using E6 specific primers. 7/27 (26%) SCC and 5/9 (55%) premalignant lesions harboured E6 DNA of which 6 (3 SCC and 3 premalignant) were negative with L1 primers suggesting possible integration of the specific viral genes or loss of other viral DNA sequences after integration of larger viral fragments. 9/10 (90%) SCC with p53 mutations were negative for E6 DNA. Our results show that both p53 alterations and HPV infection may be important etiological factors in the development of oral cancer . However, there is: i) No concordance between p53 mutations and its overexpression. ii) the presence of HPV capsid DNA (L1) does not necessarily indicate the presence of HPV oncogenic genes. iii) p53 gene mutations, but not overexpression, correlate with the absence of HPV 16-E6 and not L1 gene.

3/AB/23 (Item 3 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

02026873 3896487
T-cell proliferative response to human papillomavirus type 16 peptides: Relationship to cervical intraepithelial neoplasia
Nakagawa, M.; Stites, D.P.; Farhat, S.; Judd, A.; Moscicki, A. B.;

Canchola, A.J.; Hilton, J.F.; Palefsky, J.M.
Box 0134, Dep. Lab. Med., Sch. Med., Univ. California at San Francisco, San Francisco, CA 94143-0134, USA
CLIN. DIAGN. LAB. IMMUNOL. vol. 3, no. 2, pp. 205-210 (1996)
ISSN: 1071-412X
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Immunology Abstracts; Virology & AIDS Abstracts

The incidence of human papillomavirus (HPV)-related cervical intraepithelial neoplasia (CIN) and cervical cancer is increased with immunodeficiency, but the role of immune response, including cell-mediated immunity, in disease prevention is not well understood. In this study, T-cell proliferative responses to six synthetic peptides with predicted immunogenic determinants from the HPV -16 E4, E6, E7, and L1 open reading frames were analyzed in 22 sexually active women with new-onset CIN and 65 sexually active women without cervical disease, characterized by cytology, colposcopy, and HPV testing. T-cell proliferative responses were demonstrated to all six HPV -16 peptides. Although not statistically significant, rates of reactivity to E6 (24-45) were higher among sexually active women without disease (26%) than among women with current CIN (7%), as was the overall number of peptides stimulating a response. Women with CIN may not respond to selected HPV antigens as well as women without disease do.

3/AB/24 (Item 4 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

01640615 2853811
Skin test for HPV type 16 proteins in cervical intraepithelial neoplasia

Hoepfl, R.; Sandbichler, M.; Sepp, N.; Heim, K.; Mueller Holzner, E.; Wartusch, B.; Dapunt, O.; Jochmus Kudielka, I.; Ter Meulen, J.; et al.
Dep. Dermatol., Univ. Innsbruck, A-6020 Innsbruck, Austria
LANCET. vol. 337, no. 8737, pp. 373-374 (1991.)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Virology Abstracts

Screening tests for active and latent high-risk human papilloma virus (HPV) infections are not reliable. Classic intracutaneous (ic) tests with viral fusion proteins have not yet been used to detect HPV such tests might help to determine cell-mediated immune responses in vivo against viral proteins and thus elucidate the epidemiology and course of HPV infection. The HPV16 open-reading frames E4 and L1 (N-terminal part, L1/1/2 C-terminal part, L1/23/2) were cloned into pEX vectors, expressed in Escherichia coli C600/537 as MS2-polymerase fusion proteins, prepared by extraction with 7 mol/l urea and purified by gel extraction. Skin tests were done in volunteers, with local ethics committee approval. We conclude from these preliminary data that recombinant HPV 16 proteins can elicit clinically appreciable and specific skin reactions. These reactions are directed against the virion protein L1 and not against the E4 protein . This is noteworthy since antibodies against E4 can be detected in up to 42.6% of patients with CIN. In-vivo tests might reproduce the complex immunoreaction to HPV more exactly than in-vitro assays.

3/AB/25 (Item 5 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

01565838 2697012
Binding by immunoglobulin to the HPV-16-derived proteins L1 and E4 in cervical secretions of women with HPV-related cervical disease.
Snyder, K.A.; Barber, S.R.; Symbula, M.; Taylor, P.T.; Crum, C.P.; Roche, J.K.
Box 1005, Med. Res. 4 Build., Univ. Virginia Health Sci. Cent., Charlottesville, VA 22908, USA
CANCER RES. vol. 51, no. 16, pp. 4423-4429 (1991.)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Virology Abstracts; Immunology Abstracts

Although DNA of the human papillomaviruses (HPV) can be identified in epithelium of a large proportion of patients with genital squamous lesions, relatively little is known about the extent of the local host immune response to this virus. We analyzed cervical secretions from patients undergoing evaluation because of abnormal Papanicolaou smears (cervical biopsy showed nonspecific atypia, flat condyloma, or intraepithelial neoplasia), as well as controls, for immunoglobulin binding to proteins produced in vitro to HPV -16 L1, E4, and E7 open reading frames. We conclude that study of cervical secretions, using a quantitative assay for immunoglobulin binding to HPV -16 proteins produced in vitro, may be useful to document the quality and quantity of the immune response of the host to this important human pathogen.

3/AB/26 (Item 6 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

01143732 1761407
Identification of immunoreactive antigens of human papillomavirus type 6b by using Escherichia coli -expressed fusion proteins.
Jenison, S.A.; Firzlaff, J.M.; Langenberg, A.; Galloway, D.A.
Fred Hutchinson Cancer Res. Cent., Seattle, WA 98104, USA
J. VIROL. vol. 62, no. 6, pp. 2115-2123 (1988.)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Immunology Abstracts; Virology Abstracts

Human papillomaviruses (HPVs) are found in proliferative lesions ranging from benign condylomata to invasive carcinomas . The immunological response is poorly understood because of the lack of purified viral antigens. Bacterially derived fusion proteins expressing segments of all the major open reading frames (ORFs) of HPV -6b) have been used in Western blot (immunoblot) assays to detect antibodies against HPV -encoded proteins. The most striking reactivities present in sera from patients with genital warts were to the HPV -6b L1 ORF protein and, to a lesser extent, to the HPV -6b L2 ORF protein. Two cases of reactivity to HPV -6b E2 ORF were observed, but no reactivities were seen with other HPV -6b constructs. Two sera reacted with the HPV -16 L2 fusion protein, and two sera reacted with the HPV -16 E4 protein . The antibodies directed against the HPV -6b fusion proteins showed no cross-reactivity with comparable regions of the HPV -16 ORFs.

3/AB/27 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01767919 SUPPLIER NUMBER: 20477432 (USE FORMAT 7 OR 9 FOR FULL TEXT)
The warts and all approach to tackling cervical cancer. (genital warts and human papillomavirus)(Feature)

Bonn, Dorothy; Bradbury, Jane
The Lancet, v351, n9105, p810(1)
March 14,
1998
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0099-5355
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE:
Professional
WORD COUNT: 976 LINE COUNT: 00084

ABSTRACT: Researchers are studying the relationship between human papillomavirus (HPV) and cervical cancer , searching for ways to prevent development of the cancer . HPV , the sexually transmitted virus that causes genital warts, has emerged as a likely cause of cervical cancer . The virus induces the production of proteins which may interfere with normal growth control in cells of the cervix, leading to uncontrolled reproduction. Vaccines which target these HPV proteins may be useful in preventing cervical cancer . A new test in Europe can detect HPV in Pap smears, which may improve diagnosis.

3/AB/28 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01698581 SUPPLIER NUMBER: 19353738 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Antibody responses to HPV16 virus-like particles in women with cervical intraepithelial neoplasia infected with a variant HPV16.(Research Letters)
Ellis, J.R.M.; Etherington, I.; Galloway, D.; Luesley, D.; Young, L.S.
The Lancet, v349, n9058, p1069(2)
April 12,
1997
PUBLICATION FORMAT: Magazine/Journal ISSN: 0099-5355 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 887 LINE COUNT: 00074

3/AB/29 (Item 3 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01601340 SUPPLIER NUMBER: 17252639 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Direct DNA may be vaccine strategy for HPV.(human papillomavirus immunity)
Boyles, Salynn
Cancer Biotechnology Weekly, p8(2)
August 14,
1995
PUBLICATION FORMAT: Magazine/Journal LANGUAGE: English RECORD TYPE:
Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 383 LINE COUNT: 00037

3/AB/30 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

013587904
WPI Acc No: 2001-072111/200109
XRAM Acc No: C01-020462
New T cell epitopes from the papilloma virus L1 protein, useful for

detecting or inducing an immune response, e.g. in vaccines
Patent Assignee: MEDIGENE AG (MEDI-N)
Inventor: JOCHMUS I; NIELAND J
Number of Countries: 022 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
DE 19925199	A1	20001207	DE 1025199	A	19990601	200109	B
WO 200073335	A1	20001207	WO 2000EP5006	A	20000531	200109	

Priority Applications (No Type Date): DE 1025199 A 19990601
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
DE 19925199	A1		24	C07K-007/04	
WO 200073335	A1	G		C07K-014/025	

Designated States (National): AU CA JP US
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Abstract (Basic): DE 19925199 A1
Abstract (Basic):

NOVELTY - T cell epitopes (A) of the human papilloma virus L1 protein with any of 12 sequences and/or their functionally active variants, are new.

DETAILED DESCRIPTION - The 12 sequences are:
ILVPKVSGL;
RLVWACVGV;
HLFNRAGTV;
YLRREQMFV;
TLQANKSEV;
ILEDWNFGL;
SLWLPSEATVYL;
NLASSNYFPT;
TLTADVMTYL;
YLPPVPVSKV;
YDLQFIFQL; and
ICWGNQLFV.

INDEPENDENT CLAIMS are also included for the following:
(a) compounds (I) containing an (A) provided it is not a natural L1 protein or an exclusively N- or C-terminal deletion variant of natural L1;
(b) nucleic acid (II) that encodes (A) or (I);
(c) vector, particularly an expression vector, that contains (II);
(d) cells that contain, and preferably present, (A);
(e) complex of (A) or (I) with at least one additional molecule (III);
(f) in vitro detection of T cell activation by a compound containing at least one (A);
(g) preparing cells of (d); and
(h) test system for in vitro detection of T cells.

ACTIVITY - Antiviral; antitumor.

MECHANISM OF ACTION - Induction of a specific T cell-mediated immune response.

USE - (A), also compounds or complexes containing it or nucleic acid or vectors encoding it, is used for detection of an immune response, particularly detecting L1-specific cytotoxic T cells or to determine the L1 protein -specific antigenicity of compounds and complexes that contain (A), and for inducing a protective immune response against papilloma virus and related tumors , particularly as vaccines.

pp; 24 DwgNo 0/3

3/AB/31 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

013578373
WPI Acc No: 2001-062580/200108
XRAM Acc No: C01-017626
New T cell epitopes from the papilloma virus L1 protein, useful for detecting or inducing an immune response, e.g. in vaccines
Patent Assignee: DKFZ DEUT KREBSFORSCHUNGSZENTRUM (DKFZ-N); MEDIGENE AG (MEDI-N); DEUT KREBSFORSCHUNGSZENTRUM (DEKR-N)
Inventor: FAATH S; JOCHMUS I; NIELAND J; OSEN W; SCHAEFER K
Number of Countries: 022 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
DE 19925235	A1	20001207	DE 1025235	A	19990601	200108	B
WO 200073464	A1	20001207	WO 2000EP5005	A	20000531	200108	

Priority Applications (No Type Date): DE 1025235 A 19990601
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
DE 19925235	A1		25	C07K-007/06	
WO 200073464	A1	G		C12N-015/37	

Designated States (National): AU CA JP US
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Abstract (Basic): DE 19925235 A1
Abstract (Basic):

NOVELTY - T cell epitopes (A) of the human papilloma virus L1 protein with either of the two sequences, both comprising 9 amino acids and/or their functionally active variants, are new. All sequences are fully defined in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) compounds (I) containing an (A) provided it is not a natural L1 protein nor an exclusively N- or C-terminal deletion variant of natural L1;

(b) nucleic acid (II) that encodes (A) or (I);

(c) vector, particularly an expression vector, that contains (II);

(d) cells that contain, and preferably present, (A);

(e) complex of (A) or (I) with at least one additional molecule (III);

(f) in vitro detection of T cell activation by a compound containing at least one (A);

(g) preparing cells of (d); and

(h) test system for in vitro detection of T cells.

ACTIVITY - Antiviral; antitumor.

MECHANISM OF ACTION - Induction of a specific T cell-mediated immune response.

USE - (A), also compounds or complexes containing it or nucleic acid or vectors encoding it, is used for detection of an immune response, particularly detecting L1-specific cytotoxic T cells or to determine the L1 protein -specific antigenicity of compounds and complexes that contain (A), and for inducing a protective immune response against papilloma virus and related tumors , particularly as vaccines.

pp; 25 DwgNo 0/5

3/AB/32 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI

013565753
WPI Acc No: 2001-049960/200106
XRAM Acc No: C01-013768
XRPX Acc No: N01-038281
Detecting antigen-specific immune response, comprising capsomer, capsid, VLP (virus like particles) and/or CVLP (chimeric papillomavirus-like particles), pre-incubated antigen-presenting target cell and effector cell, useful in diagnosis
Patent Assignee: MEDIGENE AG (MEDI-N)
Inventor: JOCHMUS I; NIELAND J
Number of Countries: 022 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200073790	A1	20001207	WO 2000EP5003	A	20000531	200106 B
DE 19925234	A1	20001214	DE 1025234	A	19990601	200106

Priority Applications (No Type Date): DE 1025234 A 19990601
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200073790	A1	G	72	G01N-033/50	
				Designated States (National): AU CA JP US	
				Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE	
DE 19925234	A1			C12N-005/10	

Abstract (Basic): WO 200073790 A1
Abstract (Basic):

NOVELTY - A test system for in vitro detection of an antigen-specific immune response comprising at least 1 component (I) selected from capsomers, stable capsomers, capsids, virus-like particles (VLP's) and/or chimeric papillomavirus -like particles (CVLP's) and at least 1 antigen-presenting target cell which has been incubated with (I) and effector cells from the immune system.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) a variant on the above system, comprising (I) and at least 1 predendritic cell and/or CD16-positive cell which has been incubated with component (I), where the binding of (I) to the cells is measured;

(b) cells which, after in vitro incubation with (I), contain (and preferably present) proteins and/or protein fragments from (I);

(c) the preparation of target cells as in (b) by incubating the appropriate cell in vitro with (I);

(d) the preparation of the test systems comprising:

(i) preparing (I) by genetic engineering then incubating with predendritic and/or CD16-positive cells;

(ii) preparing (I) as in (i) and target cells as in (c) and using as effector cells an immune cell line and/or cultured primary immune cells (preferably of murine or human origin); or

(iii) preparing (I) in bacteria (e.g. Escherichia coli), yeasts (e.g. Saccharomyces cerevisiae), insect cells (e.g. from Spodoptera frugiperda or Trichoplusia ni) or mammalian cells (e.g. COS or HeLa cells); and

(e) a diagnostic system containing at least 1 test system and/or cell as described above, optionally together with a carrier (specifically a solution, a solid matrix and/or an adjuvant).

USE - The test systems are useful in the in vitro detection of activation of effector cells of the immune system by (I), specifically

for:
(1) quality control of prophylactic and/or therapeutic vaccines containing (I) or cells;
(2) identification of epitopes, peptides or protein fragments which elicit an immune response, especially a cellular immune response;
(3) monitoring the immune status of an organism towards a stimulus (especially a stimulus which is difficult to detect);
(4) monitoring a vaccination;
(5) identifying HLA (human leukocyte antigen)-haplotypes which mediate immunity towards a specific stimulus;
(6) differentiating and characterizing autoimmune diseases with respect to different autoimmune antigens; or
(7) differentiating tumor types with respect to different tumor antigens.
ADVANTAGE - The test system is easier and less expensive to handle than prior art systems based on vaccinia and adenoviruses, and allows quantitative determination of the immune response of cytotoxic T-cells. Differentiation between immune cells is possible. The uptake of antigens in the cells is independent of major histocompatibility complex molecules. No viral infection associated with viral protein expression and viral replication takes place. The system can be standardized.
pp; 72 DwgNo 0/10

3/AB/33 (Item 4 from file: 351)
DIALOG(R)File 351:Derwent WPI

013228167
WPI Acc No: 2000-400041/200034
XRAM Acc No: C00-120833
Chimeric protein comprising a papillomavirus L1 or L2 protein and a biotin-binding polypeptide, useful for delivering substances such as proteins, nucleic acids and lipids into cells, particularly papillomavirus infected cells
Patent Assignee: UNIV LOYOLA CHICAGO (LOYO)
Inventor: KAST W M; MUELLER M; NIELAND J D; VELDERS M P
Number of Countries: 088 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200031128	A1	20000602	WO 99US27555	A	19991122	200034	B
AU 200018253	A	20000613	AU 200018253	A	19991122	200043	

Priority Applications (No Type Date): US 99413611 A 19991006; US 98109510 A 19981123
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200031128	A1	E	22	C07K-014/025	

Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 200018253	A		C07K-014/025	Based on patent WO 200031128

Abstract (Basic): WO 200031128 A1
Abstract (Basic):
NOVELTY - A chimeric protein (P1) comprising a papillomavirus L1 or L2 protein (I) and a biotin-binding polypeptide (II).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a capsomere comprising P1;

(2) a papillomavirus comprising P1

(3) a virus-like particle (VLP) comprising P1;

(4) a complex comprising the capsomere, papillomavirus or VLP and a biotinylated compound; and

(5) a method for delivering a biotinylated compound into a cell comprising:

(a) forming a complex between the biotinylated compound and a capsomere, papillomavirus , or VLP comprising P1; and

(b) exposing the cell to the complex.

ACTIVITY - Cytostatic; antiviral.

MECHANISM OF ACTION - Gene therapy or vaccine.

USE - P1 is useful for delivering a wide variety of biotinylated substances (proteins, nucleic acids and lipids) into cells, particularly papillomavirus infected cells. P1 may also be used as a vaccine when the biotinylated substance is a viral antigen (e.g. papillomavirus E2 or E7 protein). P1 may be useful for treating tumors or other papillomavirus -related lesions when the substance is a cytotoxin, chemotherapeutic agent, radioactive agent, or a gene encoding a cytokine or interleukin (IL).

In standard phosphate buffered saline (PBS), three concentrations of biotinylated papillomavirus E7 peptide were incubated with either 152 or 169 capsomeres at 37 degrees C for two hours. Subsequently, C57 B1/6 splenocytes were added to the particles. These preparations, as well as a preparation of the biotinylated E7 polypeptide alone, were introduced into a culture plate containing anti C3 T cells (an E7-specific cytotoxic T lymphocyte (CTL) clone). The following day, supernatants were harvested and assayed for the presence of tumor necrosis factor alpha (TNFalpha) via a standard Wehi assay. The presence of TNFalpha was indicative of internalization and processing of the E7 protein . The results revealed that TNFalpha concentration was not markedly changed upon exposure of the cells to any concentration of E7 protein alone or the preparation of the biotinylated E7 protein and the 152 capsomeres. However, TNFalpha concentration was markedly elevated upon exposure of the cells to all concentrations of the preparation of the biotinylated E7 protein and the 169 capsomeres. The results indicated that the capsomeres including chimeric biotin-binding papillomavirus L1 proteins were able to mediate the uptake and processing of the protein by cells.

pp; 22 DwgNo 0/0

3/AB/34 (Item 5 from file: 351)
DIALOG(R)File 351:Derwent WPI

012891257
WPI Acc No: 2000-063092/200006
Related WPI Acc No: 2000-053887
XRAM Acc No: C00-017695
Fusion proteins comprising papillomavirus specific proteins useful for vaccinating against malignant tumors of the anogenital tract such as cervical carcinomas
Patent Assignee: MEDIGENE GMBH (MEDI-N)
Inventor: BURGER A; HALLEK M
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
CA 2229955	A1	19990820	CA 2229955	A	19980220	200006	B

Priority Applications (No Type Date): CA 2229955 A 19980220
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
CA 2229955 A1 E 46 C12N-015/62

Abstract (Basic): CA 2229955 A1
Abstract (Basic):

NOVELTY - A fusion protein (I) comprising 2 amino acids sequences ((Ia) and (Ib)) from 2 different papillomavirus specific (PVS) proteins ((A) and (B)), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid sequence (I') encoding (I); and

(2) a method of making (I) comprising recombinant expression of (I') and isolation of (I).

ACTIVITY - Cytostatic; virucide; dermatological.

MECHANISM OF ACTION - Vaccine.

Mice were immunized with a chimeric capsomere vaccine comprising L1 and E7 PVS proteins from human papillomavirus (HPV) strain 16 and sera was collected. As positive controls, HPV16L1 virus like particles (VLPS) and bovine papillomavirus (BPV) strain 1 L1 VLPs were assayed in parallel with a chimeric capsomere preparation. To establish a positive baseline, the HPV16 or BPV1 VLPs were first incubated with or without sera collected from immunized mice after which red blood cells were added. The extent to which preincubation with mouse sera inhibited red blood cell hemagglutinization was an indication of the neutralizing capacity of the mouse sera. The experiments were then repeated using chimeric capsomeres in order to determine the neutralizing effect of the mouse sera on the vaccine. The hemagglutinization inhibition assay was carried out as follows.

One hundred microliters of heparin (1000 usp units/ml) were added to 1 ml fresh mouse blood. Red blood cells were washed three times with phosphate buffered saline (PBS) followed by centrifugation and resuspension in a volume of 10 ml. Next, erythrocytes were resuspended in 0.5 ml PBS and stored at 4 degrees Centigrade for up to 3 days. For the hemagglutinization assay, 70 microliters of the suspension was used per well on a 96-well plate.

Chimeric capsomere aliquots from CsCl gradients were dialyzed for 1 hour against 10 mM HEPES (N-(2-OH-ethyl-)piperazine-N'-(2-ethanesulfonic acid)) (pH 7.5) and 100 microliters of 2-fold serial dilutions in PBS were added to mouse erythrocytes in round-bottom 96-well microtiter plates which were further incubated for 3 - 16 hours at 4 degrees Centigrade. For hemagglutinization inhibition, capsomeres were incubated with dilutions of antibodies in PBS for 60 minutes at room temperature and then added to the erythrocytes. The level of erythrocyte hemagglutinization (and therefore the presence of neutralizing antibodies) was determined by standard methods.

In preliminary results, mouse sera generated against chimeric capsomeres comprising HPV16L1 protein in association with E7 amino acid residues 1 - 98 was observed to inhibit hemagglutinization by HPV16 VLPS, but not by BPV1 VLPS. The mouse sera was therefore positive for neutralization antibodies against the human VLPs and this differential neutralization was most likely the result of antibody specificity for epitopes against which the antibodies were raised.

USE - (I) may be administered for preventing and treating papillomavirus infections in humans and animals (claimed). Papillomaviruses are implicated in the pathology of malignant tumor formation in the anogenital tract (of these tumors , cervical cancer is the most frequent (500000 cases/year) and in the formation of

precursor lesions of cervical intraepithelial neoplasia (CIN). Papillomaviruses also cause benign genital warts such as condylomata acuminata. However, the type and severity of disease caused by the papillomavirus is dependent on the strain causing the infection.

ADVANTAGE - The vaccine formulation (I) promotes elimination of persistently infected cells in, for example, patients with cervical intraepithelial neoplasia (CIN) or cervical carcinoma . Additionally, it also serves a prophylactic purpose by protecting patients with CIN lesions from re-infection. The capsomeres can escape neutralization by preexisting anticapsid antibodies and therefore possess a longer circulating half life as compared to chimeric virus like particles. Additionally, the chimeric capsomeres provide the advantage of increased antigenicity of both protein components from which the capsomere is formed. For example, in a VLP, protein components of the underlying capsomere may be buried in the overall structure as a result of internalized positioning within the VLP itself. Similarly, epitopes of the protein components may be sterically obstructed as a result of capsomere to capsomere contact and therefore inaccessible for eliciting an immune response.

pp; 46 DwgNo 0/0

3/AB/35 (Item 6 from file: 351)
DIALOG(R)File 351:Derwent WPI

012827073
WPI Acc No: 1999-633305/199954
XRAM Acc No: C99-184892
New human papillomavirus (HPV) 68 and 70 DNA sequences, useful in the treatment of HPV infections
Patent Assignee: INST NAT SANTE & RECH MEDICALE (INRM); INST PASTEUR (INSP)
Inventor: BEAUDENON S; LONGUET M; ORTH G
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 5981173	A	19991109	US 9611650	A	19960214	199954 B
			US 9620458	A	19960215	
			US 97815667	A	19970211	

Priority Applications (No Type Date): US 97815667 A 19970211; US 9611650 A 19960214; US 9620458 A 19960215
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5981173	A		25	C12Q-001/70	Provisional application US 9611650
					Provisional application US 9620458

Abstract (Basic): US 5981173 A
Abstract (Basic):

NOVELTY - Purified human papillomavirus (HPV) 68 DNA (I) deposited at C.N.C.M. (Collection Nationale de Culture de Microorganisms) under Accession No. I-1540 and HPV70 DNA (II), are new.

DETAILED DESCRIPTION - The sequence of (I) is selected from the 1095 (N1) or 1518 (N2) basepair sequence given in the specification. (II) has 3283 basepair sequence given in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) A purified HPV -68a nucleotide sequence encoding the L1, L2, E6 or E7 protein ;

(2) A method of detecting HPV68 in a biological sample containing

nucleic acids comprises contacting the sample with a radioactively or non-radioactively labeled (I), detecting the hybrid between (I) and the nucleic acids in the sample, and correlating the presence of the hybrid with the presence of the HPV68 in the sample; and

(3) A process for producing cloned recombinant HPV DNA comprises cloning a vector into a host cell, where the vector comprises (I).

ACTIVITY - Antiviral.

MECHANISM OF ACTION - Vaccine.

USE - Fragments of the HPV68 and HPV70 DNA may be useful as primers or probes in the detection of HPV68 or HPV70 infections. Proteins produced by the HPV DNA's can be used to immunize animals against HPV68 or HPV70 infections.

pp; 25 DwgNo 0/6

3/AB/36 (Item 7 from file: 351)
DIALOG(R)File 351:Derwent WPI

012774192
WPI Acc No: 1999-580419/199949
XRAM Acc No: C99-168871
XRPX Acc No: N99-428507
Papilloma virus specific fusion proteins useful for treating PV-specific tumors
Patent Assignee: MEDIGENE AG (MEDI-N)
Inventor: BURGER A; GABELSBERGER J
Number of Countries: 024 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9948917	A2	19990930	WO 99EP1999	A	19990324	199949	B
DE 19812940	A1	19991007	DE 1012940	A	19980324	199949	
AU 9935989	A	19991018	AU 9935989	A	19990324	200009	
EP 1066321	A2	20010110	EP 99917850	A	19990324	200103	
			WO 99EP1999	A	19990324		

Priority Applications (No Type Date): DE 1012940 A 19980324
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9948917	A2	G	26	C07K-014/025	
Designated States (National): AU CA JP MX US					
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
DE 19812940	A1			A61K-038/16	
AU 9935989	A				Based on patent WO 9948917
EP 1066321	A2	G		C07K-014/025	Based on patent WO 9948917
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

Abstract (Basic): WO 9948917 A2
Abstract (Basic):

NOVELTY - Formulation comprising at least 1 late (L-) and/or at least 1 early (E -) protein from at least 1 papilloma virus (PV), a salt and optional suitable additives, and/or auxiliary agents, is new

DETAILED DESCRIPTION - A formulation comprising:

(a) at least 1 late (L-) and/or at least 1 early (E -) protein from at least 1 PV;

(b) 0.3-4 M of a salt at a pH of 7.3-7.45; and

(c) optional suitable additives and/or auxiliary agents.

An INDEPENDENT CLAIM is also included for a method for producing a formulation as above comprising cultivating a cell containing an

expression vector that encodes the fusion protein, isolating the expression product and if necessary, adding suitable additives and auxiliary agents.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine; antiviral.

USE - The formulation is useful for the prevention or treatment of HPV -specific tumors , especially larynx, cervix, penis, vulva or anal carcinomas , and for the diagnosis of infection by one or more papilloma viruses.

ADVANTAGE - The formulation of the invention is more stable than prior formulations that comprise a neutral pH in an isotonic salt solution of about 100-150 mM salt without an additive or auxiliary agent.

pp; 26 DwgNo 0/1

3/AB/37 (Item 8 from file: 351)
DIALOG(R)File 351:Derwent WPI

012774134
WPI Acc No: 1999-580361/199949
XRAM Acc No: C99-168830
Fusion proteins free of papilloma virus non-specific epitopes, useful for treating HPV-specific tumors
Patent Assignee: MEDIGENE AG (MEDI-N)
Inventor: BURGER A; HALLEK M.
Number of Countries: 024 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9948518	A2	19990930	WO 99EP1996	A	19990324	199949	B
DE 19812941	A1	19991007	DE 1012941	A	19980324	199949	
AU 9935214	A	19991018	AU 9935214	A	19990324	200009	
EP 1064014	A2	20010103	EP 99916884	A	19990324	200102	
			WO 99EP1996	A	19990324		

Priority Applications (No Type Date): DE 1012941 A 19980324
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9948518	A2	G	36	A61K-038/16	
	Designated States (National): AU CA JP MX US				
	Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE				
DE 19812941	A1			A61K-038/16	
AU 9935214	A				Based on patent WO 9948518
EP 1064014	A2	G		A61K-038/16	Based on patent WO 9948518
	Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE				

Abstract (Basic): WO 9948518 A2
Abstract (Basic):

NOVELTY - Formulation comprising at least 1 fusion protein that does not contain any papilloma virus (PV) non-specific epitopes and optional suitable additives and/or auxiliary agents, is new.

DETAILED DESCRIPTION - The papilloma virus non-specific epitope free formulation comprises:

(1) at least 1 fusion protein comprising at least 1 L1 -protein and at least 1 E -protein from at least 1 PV; and

(2) optional suitable additives and/or auxiliary agents

An INDEPENDENT CLAIM is also included for a method for producing a formulation as above comprising, cultivating a cell containing an

expression vector that encodes the fusion protein, isolating the expression product and if adding necessary suitable additives and auxiliary agents.

ACTIVITY - Cytostatic; antiviral.

MECHANISM OF ACTION - Vaccine.

USE - The formula is useful for the prevention or treatment of HPV -specific tumors , especially larynx, cervix, penis, vulva or anal carcinomas .

pp; 36 DwgNo 0/4

3/AB/38 (Item 9 from file: 351)
DIALOG(R)File 351:Derwent WPI

012457918
WPI Acc No: 1999-264026/199922
XRAM Acc No: C99-077928
Human papilloma virus (HPV) L1 fusion protein capsomers, used in vaccines against HPV infection
Patent Assignee: UNIV LOYOLA CHICAGO (LOYO)
Inventor: GISSMANN L; MUELLER M
Number of Countries: 083 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9918220	A1	19990415	WO 98US20965	A	19981006	199922	B
AU 9896846	A	19990427	AU 9896846	A	19981006	199936	
EP 1021547	A1	20000726	EP 98950930	A	19981006	200037	
			WO 98US20965	A	19981006		
NO 200001768	A	20000602	WO 98US20965	A	19981006	200039	
			NO 20001768	A	20000406		

Priority Applications (No Type Date): US 97944368 A 19971006
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9918220	A1	E	48	C12N-015/62	
	Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW				
	Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW				
AU 9896846	A			C12N-015/62	Based on patent WO 9918220
EP 1021547	A1	E		C12N-015/62	Based on patent WO 9918220
	Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE				
NO 200001768	A			A61K-000/00	

Abstract (Basic): WO 9918220 A1
Abstract (Basic):

NOVELTY - Vaccines comprising a human papilloma virus (HPV) capsomer, comprising a HPV L1 fusion protein or a HPV L1 truncated protein , are new.

DETAILED DESCRIPTION - Vaccines comprise a human papilloma virus (HPV) capsomer, where the capsomer comprises:

(a) a fusion protein comprising a HPV L1 protein adjacent amino acid residues from a second protein; or

(b) a truncated HPV L1 protein having a deletion of one or more amino acid residues necessary for formation of a virus-like particle.

ACTIVITY - Anti-viral.

MECHANISM OF ACTION - Vaccine.

USE - The vaccines can prevent or treat human papilloma virus infection (claimed). Such therapeutic vaccinations can be used for relief against, e.g. cervical carcinoma .

ADVANTAGE - Construction of chimeric proteins comprising amino acid residues from L1 protein , and e .g. E6 or E7 protein , which give rise to chimeric capsomers, combines prophylactic and therapeutic functions of a vaccine.

Capsomers can promote elimination of persistently infected cells. Capsomers can also escape neutralization by pre-existing anti-capsid antibodies, and hence possess longer circulating half-life as compared to chimeric virus-like particles.

The fusion protein, which forms the capsomer, provides increased antigenicity.

pp; 48 DwgNo 0/0

3/AB/39 (Item 10 from file: 351)
DIALOG(R)File 351:Derwent WPI

009352499
WPI Acc No: 1993-045978/199306
XRAM Acc No: C93-020729
Skin testing kit for detecting human papilloma virus infections - contains protein L1 of HPV-16, esp. used to screen for cervical neoplasia
Patent Assignee: BEHRINGWERKE AG (BEHW)
Inventor: GISSMANN L; HOPFL R; JOCHMUS-KUDIELKA I; HOEPFL R
Number of Countries: 003 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CA 2047142	A	19921118	CA 2047142	A	19910716	199306 B
JP 7280810	A	19951027	JP 91212812	A	19910730	199601
US 5665533	A	19970909	US 91729317	A	19910715	199742
			US 92975969	A	19921113	
			US 9394590	A	19930721	
			US 95408175	A	19950322	

Priority Applications (No Type Date): DE 91U6105 U 19910517
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
CA 2047142	A		10	G01N-033/569	
JP 7280810	A		3	G01N-033/569	
US 5665533	A		3	C12Q-001/70	Cont of application US 91729317 Cont of application US 92975969 Cont of application US 9394590

Abstract (Basic): CA 2047142 A

Diagnostic kit contains protein L1 of HPV16 , or immunologically active parts of it.

L1 is injected intracutaneously at 9-25(pref. 9-15 and best about 10) microg, i.e. 0.03-0.05ml protein soln. The N- or C- terminal fragments of L1 are produced as recombinant fusion proteins with MS2-polymerase.

USE/ADVANTAGE - The kit is used in a skin test to screen patients for cervical intraepithelial neoplasia (CIN). It provides an efficient and specific test for HPV16 ; positive responses are produced against L1 but not against protein E4 of HPV16 .

Dwg.0/0
Abstract (Equivalent): US 5665533 A

A method for detecting a cell-mediated immune response to human papilloma virus comprising

a. performing an intracutaneous skin test with an effective amount of protein L1 of human papilloma virus 16 or immunologically active parts thereof, and a means for administering said protein into the skin with a pharmaceutically acceptable diluent, and

b. observing reactivity to the protein on the skin at the administration site.

Dwg.0/0

3/AB/40 (Item 11 from file: 351)
DIALOG(R)File 351:Derwent WPI

008865364
WPI Acc No: 1991-369390/199150
XRAM Acc No: C91-159272
XRPX Acc No: N91-282740
Diagnosis of human papilloma virus infection and PV-carrying tumours - using synthetic peptide(s) to detect virus specific antigen-antibody complexes by immunoassay
Patent Assignee: MEDSCAND AB (MEDS-N); FERRING AB (FERR); EURO-DIAGNOSTICA AB (EUDI-N)
Inventor: CHENG H; DILLNER J; DILLNER L; CHENG H M
Number of Countries: 018 Number of Patents: 009
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9118294	A	19911128				199150	B
AU 9178890	A	19911210				199212	
FI 9205098	A	19921110	WO 91SE335	A	19910513	199306	
			FI 925098	A	19921110		
JP 6501542	W	19940217	JP 91509789	A	19910513	199412	
			WO 91SE335	A	19910513		
EP 594613	A1	19940504	EP 91909813	A	19910513	199418	
			WO 91SE335	A	19910513		
AU 668499	B	19960509	AU 9178890	A	19910513	199626	
EP 594613	B1	19971105	EP 91909813	A	19910513	199749	
			WO 91SE335	A	19910513		
DE 69128152	E	19971211	DE 628152	A	19910513	199804	
			EP 91909813	A	19910513		
			WO 91SE335	A	19910513		
US 5932412	A	19990803	US 93949836	A	19930222	199937	
			US 97934915	A	19970922		

Priority Applications (No Type Date): SE 901705 A 19900511
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9118294	A		72		
Designated States (National): AU CA FI JP US					
Designated States (Regional): AT BE CH DE DK ES FR GB GR IT NL SE					
JP 6501542	W		24	G01N-033/569	Based on patent WO 9118294
EP 594613	A1	E		G01N-033/569	Based on patent WO 9118294
Designated States (Regional): AT BE DE DK FR GB IT LU NL SE					
AU 668499	B			G01N-033/569	Previous Publ. patent AU 9178890 Based on patent WO 9118294
EP 594613	B1	E	44	G01N-033/569	Based on patent WO 9118294
Designated States (Regional): AT BE DE DK FR GB IT LU NL SE					
DE 69128152	E			G01N-033/569	Based on patent EP 594613 Based on patent WO 9118294
US 5932412	A			C12G-001/70	Cont of application US 93949836

FI 9205098 A G01N-000/00

Abstract (Basic): WO 9118294 A

A method for diagnosing the presence of human papillomavirus (HPV) infection and papillomavirus (PV) carrying tumours is claimed. The diagnosis is performed by immunoassay based on the E2, L1 or L2 protein of HPV -1; the E2 protein of HPV -5 or HPV -8; the E4 or L2 protein of HPV -6; the E4, L1 or L2 protein of HPV -11; the E7 protein from HPV -1, 6, 8, 11, 18, 31, 33 or 56; the E4, E7, L1 or L2 protein of HPV -18; the E2, L1 or L2 protein of HPV -31; the e2, E4, L1 or L2 protein or HPV -33 or any of the remaining peptides listed in the specification. The peptides may be modified, provided they are essentially similar to or reactive with antibodies against the original peptide. The immunoassay can also be based on the IgA-antibodies against the proteins and peptides (or their modifications) given in the specification. The immunoassay is pref an ELISA, an immunofluorescent assay or an immunohistocytochemical assay performed on serum or cervical secretions gathered with a brush or spatula.

USE/ADVANTAGE - To diagnose HPV infection and PV carrying tumours , esp cervical cancer , condyloma, cervical intraepithelial neoplasia (CIN), warts or squamous cell carcinoma in the skin (claimed), by the deletion of virus specific antigen-antibody complexes. The peptides have improved immunoreactivity, and are shorter and easier to produce the known peptides. (72pp Dwg.No.0/21)

Abstract (Equivalent): EP 594613 B

Method for diagnosing the presence of human papillomavirus (HPV) infection and of papilomavirous (PV) carrying tumours by immunoassay, characterised in that the detection is performed by immunoassay based on any of the peptides e.g.
CCKCEARIELVVESSADDLRAFQQLFLNTL (HPV 18, E7)
HGPKATLQDIVLHLEPQNEIPVDLLCHEQL (HPV 18, E7)
QHLPARRAEPQRHTMLCMCCKCEARIELVV (HPV 18, E7)
LCMCCKCEARIELVVESSADDLRAFQQLFL (HPV 18, E7)
ESSADDLRAFQQLFLNTLSFVCPWCASQQ (HPV 18, E7) QSVAITCQKAAPAENKDPYD (HPV 18, E7) CCQCKSTLRLCYQSTQVDIRILQELLMGSF (HPV 31, E7)
YDNDKKNTMDYTNWGEIYII (HPV 31, E2) PQTPPSPLQSCSVQTPPWTI (HPV 33, E4)
CHTCNTTVRLSVNSTASDLRTIQQLLMGTV (HPV 33, E7)
CCECKFVVQLDIQSTKEDLRVVQQLLMGAL (HPV 56, E7) or the detection of a virus specific antigen-antibody complex int he immunoassay being detected by a peptide containing the same epitope or a peptide containing substantial homology with the original peptide.
Dwg.0/21

3/AB/41 (Item 12 from file: 351)
DIALOG(R)File 351:Derwent WPI

008800631
WPI Acc No: 1991-304643/199142
XRAM Acc No: C91-131875
XRPX Acc No: N91-233398
Sero-active epitope(s) of human papilloma-virus 16 proteins - for use vaccines and diagnosis
Patent Assignee: BEHRINGWERKE AG (BEHW)
Inventor: GISSMANN L; MULLER M
Number of Countries: 017 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
EP 451550	A	19911016	EP 91104197	A	19910319	199142	B

AU 9173515	A	19910926				199146
PT 97073	A	19911031				199148
CA 2038581	A	19910921				199149
JP 4217998	A	19920807	JP 9181596	A	19910320	199238
AU 650868	B	19940707	AU 9173515	A	19910319	199431

Priority Applications (No Type Date): EP 91104197 A 19910319; EP 90105222 A 19900320
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 451550	A				
Designated States (Regional): AT BE CH DE ES FR GB GR IT LI LU NL SE					
JP 4217998	A		10	C07K-013/00	
AU 650868	B			C07K-007/06	patent AU 9173515

Abstract (Basic): EP 451550 A

The following seroreactive epitopes of HPV 16 are new.

1. (protein E4) IPKPSPWAPKK and KPSPWAPKKHRRLS
2. (protein E6) LSRHFMHQKRTAMFQDPQERPRKLPQ and AMFQDPQERPRKLPQL CTELQTTIHDIILEC
3. (protein E7 (-221)) PTLHEYMLDLQPET TDLYCYEQ, HEYMLDLQPET, TLHEYMLDLQPETTD and EYMLDLQPETTDLY
4. (protein E7 (-107)) DEIDGPAGQAEPDRAHY and GPAGQAEPDRAHYNI
5. (protein L1 (-809)) PLLNKLDDTENAS AYAANAGVDN
6. (protein L1 (-830)) ICTSICKYPN--SNAQIFNKPY and ICTSICKYPDYIKMVSEPYGDSLFFYL RREQMFVRHLFNRAGTVGENVP DDLYIKGSGSTANLASSNY FPTPSGSM-VTSDAQIFNKPY
7. (protein L1 (-842)) KHTPPAPKEDDPLKK, AIACQKHTPPAPKE DDPLKKYTFWEVNLKEK FSADLD and LKKYTFWEVNLKEKFSADLDQF.

Peptides contg one or more of the above epitopes, vaccines, MAbs to the above peptides and a diagnostic kit contg the antibodies are all claimed.

USE/ADVANTAGE - For prophylaxis, treatment and diagnosis of HPV 16 dependent diseases eg benign lesions of the anogenital tract and cancer of the uterus, cervix, penis and vulva. (15pp dwg.No.3/3)

3/AB/42 (Item 13 from file: 351)
DIALOG(R)File 351:Derwent WPI

007403160
WPI Acc No: 1988-037095/198806
XRAM Acc No: C88-016472
Expression prods. of human papilloma viruses type 16 and 18 - used for the prodn. of diagnostics for HPV16 and HPV18 infections
Patent Assignee: BEHRINGWERKE AG (BEHW)
Inventor: DURST M; OLTERSDORF T; ROWEKAMP W; SCHNEIDERG A; SCHWARZ E; SEEDORF K
Number of Countries: 013 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
DE 3625257	A	19880204	DE 3625257	A	19860725	198806	B
EP 256321	A	19880224	EP 87110347	A	19870717	198808	
AU 8776018	A	19880128				198812	
JP 63214181	A	19880906	JP 87184635	A	19870723	198841	

Priority Applications (No Type Date): DE 3624786 A 19860723; DE 3625257 A 19860725
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes

DE 3625257 A 7
EP 256321 A G
Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE

Abstract (Basic): DE 3625257 A

(A) Expression products of human papilloma visuses type 16 and 18 (HPV16 and hPV18) by genetic technology, are new. (B) Mono- and polyclonal antibodies against expression products of HPV16 and HVP18, as are diagnostics contg. these antibodies. (C) New procedures for the diagnosis of HPV16 and HPV18 infections comprise contecting biopsy material with a diagnostic contg. antibodies against expression products of HPV16 or HPV18 .

(D) DNA coding for the proteins HPV18 E1-, E6-, E6-, E7 - and L1 -protein is new, as it is use for the prodn. of these proteins by genetic technology methods. (E) New diagnostics contain DNA coding for hPV16 or HPV18 expression products or a part of this DNA, and in a new procedure for the diagnosis of HPV16 and HPV18 infections the RNA or DNA to be investigated is hybridiced with such DNA or a part there of. (F) The expression vectors pEX8-mer, pEx 10 mer and pEX 12-mer are new, as are hybrid vectors containing the DNA of one of these vectors in the polylinker segment.

USE - The new expression products can be used for the prodn. of antibodies. The antibodies and the new DNA can be used for the early diagnosis of HPV16 and HPV18 infections HPV16 and HPV18 infections are associated with alignment genital tumours .

3/AB/43 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0238036 DBA Accession No.: 99-08137 PATENT
Human papilloma virus (HPV) L1 fusion protein capsomers, used in vaccines against HPV infection- recombinant vaccine preventing against cervix carcinoma
AUTHOR: Gissmann L; Mueller M
CORPORATE SOURCE: Chicago, IL, USA.
PATENT ASSIGNEE: Univ.Chicago-Loyola 1999
PATENT NUMBER: WO 9918220 PATENT DATE: 990415 WPI ACCESSION NO.: 99-264026 (9922)
PRIORITY APPLIC. NO.: US 944368 APPLIC. DATE: 971006
NATIONAL APPLIC. NO.: WO 98US20965 APPLIC. DATE: 981006
LANGUAGE: English
ABSTRACT: Vaccines comprising a human papilloma virus (HPV) capsomer, comprising a HPV L1 fusion protein or a HPV L1 truncated protein are claimed. The capsomer comprises: a fusion protein of HPV L1 protein adjacent to amino acid residues from a 2nd protein (E6 or E7 protein) or a truncated HPV L1 protein with a deletion of one or more amino acid residues needed for formation of a virus-like particle. The vaccines can prevent or treat HPV infection (claimed). These therapeutic vaccines can be used against cervix carcinoma . The chimeric capsomers combine prophylactic and therapeutic activities of a vaccine. The capsomers can promote elimination of persistently infected cells and can escape neutralization by pre-existing anti-capsid antibodies and possess longer circulating half-life as compared to chimeric virus-like particles. The fusion protein, which forms the capsomer, provides increased antigenicity. (48pp)

3/AB/44 (Item 2 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs

0225212 DBA Accession No.: 98-06809 PATENT
Attenuated strain of bacterium expressing papilloma virus major capsid protein - recombinant vaccine
AUTHOR: Kiddle S J
CORPORATE SOURCE: Lausanne, Switzerland.
PATENT ASSIGNEE: Found.Perfect.Res.Gynecol.Obstet.Lausanne 1998
PATENT NUMBER: WO 9815631 PATENT DATE: 980416 WPI ACCESSION NO.: 98-240817 (9821)
PRIORITY APPLIC. NO.: GB 9621091 APPLIC. DATE: 961009
NATIONAL APPLIC. NO.: WO 97GB2740 APPLIC. DATE: 971007
LANGUAGE: English
ABSTRACT: An attenuated prokaryote (A) transformed with nucleic acid (I) encoding papilloma virus (PV) major capsid protein (II), which assembles in (A) to form virus-like particles (VLP) is claimed. (A) are useful for vaccination, particularly mucosal, to prevent or treat PV infections or related cancers of the anogenital tract (particularly the cervix). VLPs are also used, when immobilized, for detecting antibodies specific for PV. Properly assembled VLP, essential for antibody induction can now be produced in attenuated bacteria. They induce a human PV-specific, conformation-dependent and neutralizing antibody response in serum and genital secretions, and also induce cytotoxic T-lymphocytes able to kill cells already infected with human PV. (A) are administered to the oral, nasal, rectal or genital mucosa. The preferred microorganism is Salmonella typhimurium, Salmonella typhi, Salmonella dublin, Salmonella enteriditis, Escherichia coli, Shigella, Yersinia, Lactobacillus, Mycobacterium, or Listeria spp. (II) is derived from human PV strains 16, 18, 31, 45, or 56 and particularly is the L1 protein (optionally as a fusion protein with L2), E6 , E7 or E2.

3/AB/45 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0222866 DBA Accession No.: 98-04463 PATENT
Infectious papilloma virus pseudoviral particle- for vector-mediated gene transfer and e.g. hemophilia and cancer gene therapy
AUTHOR: Lowy D R; Schiller J T; Roden R B
CORPORATE SOURCE: Rockville, MD, USA.
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 1998
PATENT NUMBER: WO 9802548 PATENT DATE: 980122 WPI ACCESSION NO.: 98-110595 (9810)
PRIORITY APPLIC. NO.: US 22104 APPLIC. DATE: 960717
NATIONAL APPLIC. NO.: WO 97US12115 APPLIC. DATE: 970714
LANGUAGE: English
ABSTRACT: An infectious papilloma virus pseudovirus particle (I) is new. Also claimed are: a human papilloma virus-16 (HPV -16) virion; an infectious (I) containing a papilloma virus vector DNA which contains an E2 binding site and an expression cassette containing a gene and a sequence controlling gene expression, and a papilloma virus capsid which contains L1 and L2 structural proteins such that the capsid encapsidates the vector DNA, where the gene is derived from a first biological species and the L1 structural protein is derived from a second different biological species; and a cell line containing (I). (I) can be used as a vector for gene transfer into mammal cell cultures. It can also be used for providing a human with a therapeutic protein, or an immunogenic protein , e .g. Factor-IX or herpes

simplex virus thymidine-kinase (EC-2.7.1.21). (I) can also be used for inherited and acquired disease therapy and gene therapy. Diseases include AIDS, cancer , cystic fibrosis, muscular dystrophy, Parkinson disease, psoriasis and atopic dermatitis etc. (41pp)

3/AB/46 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0221166 DBA Accession No.: 98-02763 PATENT
Virus-like particle comprising DNA in papilloma virus capsid- for use as recombinant vaccine and in gene therapy
AUTHOR: Bloch M A
CORPORATE SOURCE: Lyon, France.
PATENT ASSIGNEE: Pasteur-Merieux-Sera+Vaccines 1997
PATENT NUMBER: WO 9746693 PATENT DATE: 971211 WPI ACCESSION NO.: 98-042201 (9804)
PRIORITY APPLIC. NO.: FR 967174 APPLIC. DATE: 960604
NATIONAL APPLIC. NO.: WO 97FR962 APPLIC. DATE: 970603
LANGUAGE: French
ABSTRACT: A new non-infectious virus-like particle (VLP) contains a capsid that defines an internal space and consists of at least part of the L1 protein , preferably a chimeric L1 - E7 protein , of human papilloma virus, and a papilloma virus nucleic acid lacking a portion of the genomic regions encoding wild-type late regions, contained in the capsid. The VLP can be used as a vehicle for gene transfer in gene therapy, immunotherapy or vaccination against cancer and infection. The nucleic acid preferably encodes a cytokine, an accessory molecule facilitating cellular recognition by helper T-lymphocytes, a tumor -associated antigen or a parasitic, virus or bacterium antigen. The VLP is produced by mixing the components together in the presence of a calcium salt. The capsid is preferably produced by recombinantly expressing the capsid proteins in baculo virus-infected insect cell culture and treating isolated capsids with a Ca2+-chelating agent. (24pp)

3/AB/47 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0206840 DBA Accession No.: 97-01961 PATENT
Recombinant adeno virus with complete E1 and functional E3 gene deletion- rabies virus, respiratory-syncytial virus, human papilloma virus, HIV virus or tumor-associated antigen expression for recombinant vaccine construction
AUTHOR: Ertl H C; Wilson J M
CORPORATE SOURCE: Philadelphia, PA, USA.
PATENT ASSIGNEE: Wistar-Inst.; Univ.Pennsylvania 1996
PATENT NUMBER: WO 9639178 PATENT DATE: 961212 WPI ACCESSION NO.: 97-042858 (9704)
PRIORITY APPLIC. NO.: US 78 APPLIC. DATE: 950608
NATIONAL APPLIC. NO.: WO 96US9495 APPLIC. DATE: 960605
LANGUAGE: English
ABSTRACT: A new recombinant adeno virus (Ad, e.g. Adrab.gp) has a complete deletion of the E1 gene and at least a functional deletion of the E3 gene, and contains (at the E1 deletion site) a non-Ad promoter for expression of a heterologous gene from a disease-causing agent, to produce a recombinant vaccine conferring a complete protective immune response at low dosage. The promoter may be from cytomegalo virus (e.g.

an enhancer-promoter), respiratory-syncytial virus (RSV) or SV40 virus. The gene may encode a rabies virus Evelyn Rockitniki Abelseth glycoprotein or G-protein (preferred), RSV glycoprotein or fusion protein, human papilloma virus E6, E7 or L1 protein , HIV virus gp120, or a tumor -associated antigen. The Ad may be administered at 10,000-10,000,000 pfu by an s.c., rectal, intratracheal, i.m. or intranasal route. Complete and functional deletion of E1 and E3 genes renders the recombinant Ad replication-defective. (57pp)

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?ds

Set	Items	Description
S1	117	(PAPILLOMA? OR HPV?) AND PROTEIN(2N)E? ? AND PROTEIN(2N) L1?
S2	96	RD (unique items)
S3	47	S2 AND (CANCER? OR CARCINO? OR MALIG? OR TUMOR? OR TUMOUR? OR NEOPLAS?)
S4	508	(PAPILLOMA? OR HPV?) AND (CANCER? OR CARCINO? OR MALIG? OR TUMOR? OR TUMOUR? OR NEOPLAS?) AND FUSION(W)PROTEIN? AND (LARYNX? OR THROAT? OR GENITAL? OR CERVI? OR PENIS OR VULVA OR ANUS?)
S5	109	S4 AND (CAPSID? OR CAPSOMER?)
S6	41	RD (unique items)
S7	34	S6 NOT S3

?t s7/3 ab/1-34

7/AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10358087 20179467
Human papillomavirus vaccines.
Breitburd F; Coursaget P
Unite@a3 des Papillomavirus, Unite@a3 Mixte Institut Pasteur/INSERM U190, Institut Pasteur, 25 rue du Docteur Roux, Paris, 75015, France.
Seminars in cancer biology (UNITED STATES) Dec 1999, 9 (6) p431-44, ISSN 1044-579X Journal Code: A6Y
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

Genital human papillomavirus (HPV) infections are the viral sexually transmitted diseases most frequently diagnosed that include anogenital condylomas and squamous intra-$bepithelial lesions, among which the precursors of invasive carcinomas of the uterine cervix . In animal PV models, vaccination against L1 and/or L2 viral capsid proteins provides an efficient protection against infection, involving virus type-specific neutralizing antibodies. Vaccination against non-structural E1, E2, E6 or E7 viral proteins does not prevent infection, unless administered altogether, but tends to stimulate regression, warranting the design of therapeutic vaccines. Prophylactic vaccines based on the use of virus-like particles (VLPs) obtained by auto-assembly of L1 or L1 and L2 proteins produced by recombinant DNA technology are under phase I/II clinical trials for HPV6 /11 associated with condylomas and for HPV16 , the most frequent oncogenic genotype. Second generation vaccines are chimeric proteins or VLPs incorporating one of the structural proteins (L1 or L2) fused to a non-structural protein (E6, E7 or E2), which should induce both humoral and cellular immunity. Vaccine valency (number of genotypes), route of administration (humoral versus local immunity), vaccinees (children, young adults, gender) and forms of vaccines (recombinant $LSalmonella typhimurium*I$L, edible plants expressing L1 and L2 proteins, DNA vaccines, synthetic antigenic peptides) are under study. End points to evaluate vaccine efficacy in phase III trials should include

viral DNA detection and typing, and screening for low or high grade intraepithelial lesions. Therapeutic vaccines based on recombinant HPV E6 and/or E7 vaccinia virus, L2-E7 fusion proteins or E7 peptides corresponding to cytotoxic T cell epitopes are currently tested (phase I/II trials) in patients with cervical carcinomas of advanced clinical stages or high grade intraepithelial lesions. Animal studies, phase I/II clinical trials and implementation of the community support that HPV vaccines will constitute an efficient means to prevent carcinoma of the uterine cervix . Copyright 2000 Academic Press.

7/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08759797 96335695
Proliferative T cell responses to the human papillomavirus type 16 E7 protein in women with cervical dysplasia and cervical carcinoma and in healthy individuals.
Luxton JC; Rowe AJ; Cridland JC; Coletart T; Wilson P; Shepherd PS
Department of Immunology, Guy's Hospital Medical School, London, UK.
Journal of general virology (ENGLAND) Jul 1996, 77 (Pt 7) p1585-93, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The levels of proliferative T cell responses to peptides representing the human papillomavirus type 16 (HPV -16) E7 protein have been measured using short-term T cell lines derived from peripheral blood of healthy women and those with cervical dysplasias and carcinoma of the cervix . In healthy individuals 47 percent (7/15) responded predominantly to the N- and C-terminal regions of the protein and 6/7 responders were to a single peptide between amino acids 80-94. In comparison 29 percent (9/31) of women with cervical dysplasia responded to HPV -16 E7, with a significantly reduced response to both the N- and C-terminal regions (P = 0.03 and 0.038, respectively). A higher proportion of responders was found in patients with high grade lesions (56 percent, 5/9) versus those with atypical or low grade histology (20 percent, 4/20) and the response to a single peptide between amino acids 75-94 was also increased in this patient group (P = 0.044). This may be a reflection of higher levels of current or previous exposure to HPV -16 in patients with high grade lesions. Correlation of T cell responses with HPV DNA type (detected by PCR of cervical biopsy tissue) showed that 3/9 (33 percent) HPV -16 DNA-positive individuals responded. This suggests that E7 may not be the dominant target of the immune response or that the response to E7 is down-regulated in these patients. In addition 4/18 (22 percent) HPV -16 DNA-negative individuals responded, suggesting that their T cells may have been primed by previous exposure to HPV -16 or that a cross-reactive response was detected. Proliferative T cell responses to both HPV -16 E7 and L1 were reduced in women with cervical carcinoma in comparison to those with cervical dysplasia and healthy controls. The observed down-regulation of responses to HPV -16 E7 in women with cervical dysplasia and cervical carcinoma may reflect an altered functional balance between subsets of T helper cells in HPV -16 infections.

7/AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08641063 96203946
Proliferative T cell responses to human papillomavirus type 16 L1

peptides in patients with cervical dysplasia.
Shepherd PS; Rowe AJ; Cridland JC; Coletart T; Wilson P; Luxton JC
Department of Immunology, Guy's Hospital Medical School, UMDS, London, UK. p.shepherd@uk.ac.umds.miranda
Journal of general virology (ENGLAND) Apr 1996, 77 (Pt 4) p593-602, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Human papillomavirus type 16 (HPV -16) can cause genital warts, cervical dysplasias and carcinoma of the cervix . Cell-mediated immunity is thought to be important in protection against the virus and in its elimination, but little is known about the mechanisms involved. In a cross-sectional study we have demonstrated proliferative T cell responses to peptides representing the HPV -16 L1 capsid protein (aa 199-409) in the peripheral blood of 63% of patients (n = 41) with histological evidence of cervical dysplasia and in 45% of healthy age-matched controls (n = 11). This was achieved by generating short-term T cell lines (STLs) from each individual in vitro against a beta-galactosidase-HPV - 16 L1 (aa 199-409) fusion protein for 2 weeks, and then identifying the HPV epitopes they recognized with overlapping synthetic peptides (15-mers) spanning this region in 3 day specificity assays. Histological grading and HPV typing by PCR were performed on patients' cervical biopsies taken at the same clinical visit as the peripheral blood samples. An immunogenic region was identified between aa 311-345 in 73% of patients (18% in controls) who responded to HPV -16 L1 (aa 199-409). The number of responders to this region was significantly higher in patients with HPV -16-positive biopsies when compared to those with HPV -16-negative biopsies (P = 0.006), as was the number of responders to individual peptides 311-325 (NLASSNYFPTPSGSM; p = 0.04) and 321-335 (PSGSMVTSDAQIFNK; P = 0.004) representing this region. The mean level of response to each individual peptide was also higher in the patient group than the controls (P < 0.05). The most significant finding was that all patients with evidence of a current HPV -16 infection responded to one or more L1 peptides (P = 0.0004) and 92% had high grade cervical intraepithelial neoplasia (CIN III). We also found that the CIN III group was more likely to respond to any L1 peptide than either the atypical group (P = 0.04) or the controls (P = 0.05). Data from four individuals showed that the majority of peptide-specific STLs were CD4+ but some CD8+ STLs were also detected.

7/AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08481961 96129547
Perinatal infection and persistence of human papillomavirus types 16 and 18 in infants.
Cason J; Kaye JN; Jewers RJ; Kambo PK; Bible JM; Kell B; Shergill B; Pakarian F; Raju KS; Best JM
Richard Dimbleby Laboratory of Cancer Virology, Department of Virology, Rayne Institute, London, United Kingdom.
Journal of medical virology (UNITED STATES) Nov 1995, 47 (3) p209-18, ISSN 0146-6615 Journal Code: I9N
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Perinatal transmission of genital human papillomaviruses (HPVs), including HPV -16 and -18 which are associated with anogenital carcinomas have been described previously [Pakarian et al. (1994): British Journal of Obstetrics and Gynaecology 101:514-517; Kaye et al. (1994) Journal of Medical Virology 44:415-421]. A study was undertaken to investigate whether

HPV -16 and -18 DNA in infants contaminated at delivery persists until they are 6 months of age. Of 61 pregnant women recruited, 42 (68.8%) were HPV -16 and 13 (21.3%) were HPV -18 DNA positive. At 24 hr there were transmission rates from HPV DNA positive mothers to their infants of about 73% (HPV -16: 69%; HPV -18: 76.9%). Ten mothers who were both HPV -16 and -18 DNA positive produced six (60%) infants who were also doubly positive at 24 hr. HPV DNA persisted to 6 weeks in 79.5% (HPV -16: 84%; HPV -18: 75%) of those infants who were positive at birth. At 6 months of age, persistent HPV -16 DNA was detected in 83.3% of cases, but HPV -18 DNA persistence at this time was 20%. To extend these observations over a greater age range of children HPV -16 L1 and L2 proteins were expressed in insect cells via recombinant baculoviruses and sera from 229 children were examined to determine at what age IgM antibodies to HPV were acquired. There was a bimodal distribution of IgM seropositivity which peaked between 2 and 5 and 13 and 16 years of age, suggesting that two distinct modes of transmission may occur. The observation that infection with high cancer risk genital HPVs may occur in early life and persist is of considerable importance for HPV vaccine strategies.

7/AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08434939 96068799
Conformational and linear epitopes on virus-like particles of human papillomavirus type 33 identified by monoclonal antibodies to the minor capsid protein L2.
Volpers C; Sapp M; Snijders PJ; Walboomers JM; Streeck RE
Institut fur Medizinische Mikrobiologie, Johannes-Gutenberg-Universitat Mainz, Germany.
Journal of general virology (ENGLAND) Nov 1995, 76 (Pt 11) p2661-7, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The organization of epitopes on the minor capsid protein L2 of human papillomavirus (HPV) type 33 has been analysed using three monoclonal antibodies (MAbs) generated against a large fragment of the L2 protein (amino acids 82-259) expressed as a glutathione S-transferase fusion protein . The topology of the L2 epitopes has been investigated with respect to the structure of HPV -33 virus-like particles (VLPs). Two of the MAbs reacted with linear epitopes which were mapped to amino acids 153-160 and 163-170, respectively. These epitopes were accessible in denatured but not in native VLPs consisting of L1 and L2, suggesting an internal location. The third antibody was unable to detect denatured L2 protein but reacted with native VLPs. This is the first demonstration of an apparent conformational epitope of the HPV L2 protein. A model for the putative orientation of L2 in the papillomavirus capsid is deduced from the location of these and other antigenic sites.

7/AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08075159 95088581
Analysis of type-restricted and cross-reactive epitopes on virus-like particles of human papillomavirus type 33 and in infected tissues using monoclonal antibodies to the major capsid protein.
Sapp M; Kraus U; Volpers C; Snijders PJ; Walboomers JM; Streeck RE
Institut fur Medizinische Mikrobiologie, Johannes-Gutenberg-Universitat

Mainz, Germany.
Journal of general virology (ENGLAND) Dec 1994, 75 (Pt 12) p3375-83, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A panel of six monoclonal antibodies recognizing at least three different antigenic regions has been raised against the L1 major capsid protein of human papillomavirus type 33 (HPV -33), which is associated with cervical carcinoma . The antigenic sites defined by these antibodies have been mapped and classified as type-restricted or broadly cross-reactive using bacterially expressed L1 fusion proteins of a variety of HPV types. Conformational and linear epitopes have been distinguished using native and denatured virus-like particles. HPV infection of genital lesions has been analysed using both monoclonal antibodies and DNA amplification by PCR. The antibodies obtained should be useful to probe the structure of HPV capsids and to develop a general assay for the detection and classification of productive HPV infections.

7/AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08050716 95053930
Brief report: antibody response to E6, E7, and L1 proteins of human papillomavirus 16 in an Italian population.
Di Lonardo A; Campo MS; Venuti A; Marcante ML
Laboratory of Virology, CRS-Regina Elena Institute for Cancer Research, Rome, Italy.
Journal of medical virology (UNITED STATES) Aug 1994, 43 (4) p357-61, ISSN 0146-6615 Journal Code: I9N
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The serological response to human papillomavirus type 16 (HPV16) E6, E7, and L1 proteins was investigated in Italian patients with cervical cancer , cervical intraepithelial neoplasia (CIN), flat cervical warts, condylomas, and in healthy individuals. Bacterially expressed beta-galactosidase fusion proteins were purified and used as antigen in Western blot assays. The HPV16 DNA status was also determined in most of the women. The incidence of antibody response to E6 and E7 proteins was higher in cervical cancer than in CIN patients. No variation of antibody titre against E6 was observed in the cervical cancer patients, while one patient in an advanced stage of disease displayed very high levels of E7 antibodies. High seroprevalence to both E6 and L1 was observed in patients with genital condylomas, but this may be due to cross-reactivity between HPV6 or 11 antibodies and the experimental HPV16 antigens. Antibodies to L1 were detected in control women, suggesting that HPV infection is widespread. The data obtained in this study are in agreement with previous findings in other countries.

7/AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07813068 93188141
Development of type-specific and cross-reactive serological probes for the minor capsid protein of human papillomavirus type 33.
Volpers C; Sapp M; Komly CA; Richalet-Secordel P; Streeck RE
Institut fur Medizinische Mikrobiologie, Universitat Mainz, Germany.
Journal of virology (UNITED STATES) Apr 1993, 67 (4) p1927-35, ISSN

0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Human papillomavirus type 33 (HPV33) is associated with malignant tumors of the cervix . In an attempt to develop immunological probes for HPV33 infections, antisera against various bacterial fusion proteins carrying sequences of the minor capsid protein encoded by L2 were raised in animals. Antigenic determinants on the HPV33 L2 protein were identified by using truncated fusion proteins and were classified as type specific or cross-reactive with respect to HPV1 , -8, -11, -16, and -18. Cross-reactive epitopes map to amino acids 98 to 107 or to amino acids 102 to 112 and 107 to 117, respectively, depending on the fusion protein used for immunization. Antibodies directed toward these epitopes detect L2 proteins of HPV11 , -16, and -18, but not of HPV1 and -8, in Western immunoblots and enzyme-linked immunosorbent assays. HPV33 L2 amino acids 82 to 94 and 117 to 130 induce type-specific antibodies, with the major response directed to amino acids 117 to 130. By using a synthetic peptide corresponding to L2 amino acids 117 to 130, high-titered, type-specific antisera were obtained. These antisera should be useful as immunological probes for HPV33 infection.

7/AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07360248 91220714
Antibodies to human papillomavirus type-16 in human sera as revealed by the use of prokaryotically expressed viral gene products.
Kochel HG; Sievert K; Monazahian M; Mittelstadt-Deterding A; Teichmann A; Thomssen R
Centre of Hygiene and Human Genetics of the University, Department of Medical Microbiology, Gottingen, Germany.
Virology (UNITED STATES) Jun 1991, 182 (2) p644-54, ISSN 0042-6822
Journal Code: XEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Open reading frames of human papillomaviruses were expressed in Escherichia coli as beta-galactosidase fusion proteins . These bacterially derived papillomaviral gene products were used to examine sera from 67 women (63 healthy subjects, 4 patients with genital carcinoma) for antibodies to papillomavirus type-16 antigens (E1, E2, E4, E5, E6, E7, L1, L2) and the L2 proteins of HPV -6b and HPV -18 by Western-blot analysis. The serologic data were compared with cytological findings classified according to Papanicolaou and with nucleic acid hybridization data from cervical smears of the same individuals. Twenty-three of the normal individuals showed antibodies exclusively directed against L2 gene products; whereas in the sera from the four genital cancer patients, antibodies to the early gene products E4 and/or E7 could be detected. In one case these antibodies were found to be combined with antibodies to L2 of HPV -16 and -18 and in another case with those to E1 and E2 of HPV -16. In none of the sera examined could antibodies to L1, E5 or E6 be identified. Three of the antibody positive normal women were found to be also positive for HPV -16/18 DNA, while all of the 40 seronegative women were HPV -16/18 DNA negative. These data indicate that serology may be a valuable means to study the epidemiology of genital human papillomavirus infection.

7/AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07249870 93052671
Serological assays for the detection of HPV antibodies.
Galloway DA
Fred Hutchinson Cancer Research Center, Seattle, WA 98104.
IARC scientific publications (FRANCE) 1992, (119) p147-61, ISSN 0300-5038 Journal Code: GKU
Contract/Grant No.: CA42792, CA, NCI; AI29363, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
A variety of serological assays to detect antibodies to genital -type HPVs have been developed. Bacterially expressed fusion proteins , synthetic peptides and HPV 11 virus propagated in a xenograft system have been the most commonly used antigen targets in either Western blot assays or ELISAs. HPV antibodies have been readily detected and most studies suggest that they are type-specific. Primarily, antibodies appear to be directed against the capsid antigens. The presence or titre of antibodies to the HPV 16 E7 protein is strongly associated with cervical cancer in approximately 25% of cases. The significance of antibodies to other HPV antigens, or of antibodies which recognize conformational epitopes is less clear. Attempts to validate the sensitivity and specificity of serological assays are extremely preliminary, and are complicated by a lack of understanding of the natural history of papillomavirus infections.

7/AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07245390 92383549
The detection of human papillomaviruses in cervical biopsies by immunohistochemistry and in situ hybridization.
Shepherd P; Lunny D; Brookes R; Palmer T; McCance D
Department of Immunology, Guy's Hospital, UMDS, London, UK.
Scandinavian journal of immunology. Supplement (ENGLAND) 1992, 11 p69-74, ISSN 0301-6323 Journal Code: UC7
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The presence of human papillomavirus (HPV) types 6, 16 and 18 in cervical biopsies can be detected by an immunoperoxidase technique using type-restricted monoclonal antibodies raised against fusion proteins representing the L1 major capsid proteins of these three HPV types. In a retrospective study (n = 54) we have used these antibodies and biotinylated DNA probes of HPV 6, 16 and 18 to detect and type HPV in formalin-fixed material from the cervix . The biopsies were classified histologically into normals, wart infections without dysplasia, cervical intraepithelial neoplasia (CIN) and squamous cell carcinomas . Antibody staining showed that 22% of all CIN was positive for HPV 16 and 40% of cervical warts were positive for HPV 6, 16 and 18. There was no HPV capsid protein detected in the normals and squamous cell carcinomas using these antibodies, whereas 25% of the tumours were positive for HPV 16 by in situ hybridization. Sections of cervical warts and CIN positive for HPV types by in situ hybridization were also positive by antibody staining which suggests that both techniques are detecting replicating virus. We feel these two techniques complement each other in detection and typing of HPV in cervical biopsies from patients with active disease.

7/AB/12 (Item 12 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07234477 92138066
Detection of antibodies to a linear epitope on the major coat protein (L1) of human papillomavirus type-16 (HPV-16) in sera from patients with cervical intraepithelial neoplasia and children.
Cason J; Kambo PK; Best JM; McCance DJ
Richard Dimbleby Laboratory of Cancer Virology, Rayne Institute, St Thomas's Hospital, London, UK.
International journal of cancer. Journal international du cancer (UNITED STATES) Feb 1 1992, 50 (3) p349-55, ISSN 0020-7136 Journal Code: GQU
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Antibodies to the major (L1) coat protein of human papillomavirus type 16 (HPV -16) in sera from patients with cervical intra-epithelial neoplasia (CIN) have been investigated by means of recombinant proteins and synthetic peptides. When L1-HPV -16 fusion proteins were used in immunoblot assays, no antibody reactivity was found in sera from 52 patients with CIN or from 21 unrelated children. Amino-acid sequence analyses indicated that L1-HPV -16 amino acids 473 to 492 may contain an HPV -16 type-restricted epitope since the greatest diversity occurs in this region. In the ELISA, seropositivity to peptides 473 to 492 was more common among CIN patients whose biopsies contained HPV -16 DNA (91%, 21 of 23) than among their children (24%, 5 of 21; p less than 0.001) or other CIN patients with HPV -16 DNA-negative biopsies (66%, 19 of 29; p less than 0.05), but was unrelated to the severity of the CIN lesion. Antibodies to L1- HPV -16 peptide 473 to 492 among seropositive CIN patients cross-reacted with the analogous L1-HPV -33, but not with the L1-HPV -6b peptide, and were predominantly IgM. In contrast, antibodies which recognized a less variable region of L1-HPV -16 (amino acids 279 to 293) showed no association with HPV -16 DNA status. Seropositivity to the L1- HPV -6b (amino acids 473-492) was less frequent (33%) among CIN patients and unassociated with HPV -16 DNA status (p greater than 0.1); however 51% (37 of 72) of patients with genital warts had antibodies to this peptide.

7/AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06972945 91335786
Type-specific and cross-reactive epitopes in human papillomavirus type 16 capsid proteins.
Beiss BK; Heimer E; Felix A; Burk RD; Ritter DB; Mallon RG; Kadish AS
Department of Pathology, Albert Einstein College of Medicine, Bronx, New York 10461.
Virology (UNITED STATES) Sep 1991, 184 (1) p460-4, ISSN 0042-6822 Journal Code: XEA
Contract/Grant No.: CA-47630, CA, NCI; CA-13330, CA, NCI; CA-09173, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Genital human papillomavirus (HPV) 16 infection is frequently associated with cancer of the uterine cervix , as well as with precancerous lesions. In order to generate serologic reagents which might be useful in the diagnosis of HPV 16 infection, rabbit polyclonal and mouse monoclonal antisera were raised to carboxy terminal peptides from the HPV 16 L1 and L2 open reading frames (ORFs). Anti-L1 and -L2 peptide sera recognized HPV 16 L1 and L2 fusion proteins in Western blots and by immunoprecipitation. In Western blot analysis of L1 proteins from different

HPV types, antisera to the L1 peptide reacted only with HPV 16, thus identifying an HPV 16 type-specific linear epitope. Anti-L2 peptide sera reacted with L2 fusion proteins from HPVs 6 and 16, but not from BPV, thus identifying a partially cross-reactive epitope in the HPV 16 L2. Computer analysis of carboxy terminal amino acid sequences of the L1 and L2 ORFs of multiple HPV types supported the Western blot findings. Despite the HPV 16 type specificity found in Western blots, anti-L1 peptide sera identified nuclear antigen by immunocytochemistry in cervical biopsies infected with HPV 16, as well as other genital HPV types. Anti-L2 peptide sera failed to recognize antigen in infected tissue.

7/AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06965037 91140710
Characterization of human antibody-reactive epitopes encoded by human papillomavirus types 16 and 18.
Jenison SA; Yu XP; Valentine JM; Galloway DA
Fred Hutchinson Cancer Research Center, Seattle, Washington 98104.
Journal of virology (UNITED STATES) Mar 1991, 65 (3) p1208-18, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: P01-AI29363, AI, NIAID; P01-CA42792, CA, NCI; R01-CA35568, CA, NCI; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have previously reported that the most common human serum immunoglobulin G antibody reactivities to human papillomavirus type 16 and type 18 (HPV16 and HPV18)-encoded proteins are directed against the minor capsid proteins (HPV16 L2 and HPV18 L2) and to the E7 protein of HPV16 (S. A. Jenison, X.-P. Yu, J. M. Valentine, L. A. Koutsky, A. E. Christiansen, A. M. Beckmann, and D. A. Galloway, J. Infect. Dis. 162:60-69, 1990). In this study, the antibody-reactive segments of the HPV16 E7, HPV16 L2, and HPV18 L2 polypeptides were mapped by using nested sets of deleted recombinant proteins. A single major immunoreactive region was identified in the HPV16 E7 polypeptide between amino acids (aa) 21 and 34 (DLYCYE-QLNDSSEE). In contrast, three distinct immunoreactive regions of the HPV16 L2 polypeptide were present in the segment between aa149 and aa204, and three distinct immunoreactive regions of the HPV18 L2 polypeptide were present in the segment between aa110 and aa211. With the exception of one serum sample, serum immunoglobulin G antibodies which reacted with HPV16 L2 polypeptides or with HPV18 L2 polypeptides were not cross-reactive.

7/AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06923008 91330163
Binding by immunoglobulin to the HPV-16-derived proteins L1 and E4 in cervical secretions of women with HPV-related cervical disease.
Snyder KA; Barber SR; Symbula M; Taylor PT; Crum CP; Roche JK
Department of Pathology, University of Virginia Health Sciences Center, Charlottesville 22908.
Cancer research (UNITED STATES) Aug 15 1991, 51 (16) p4423-9, ISSN 0008-5472 Journal Code: CNF
Contract/Grant No.: CA47676, CA, NCI; DK35182, DK, NIDDK; DK42358, DK, NIDDK; +
Languages: ENGLISH

Document type: JOURNAL ARTICLE

Although DNA of the human papillomaviruses (HPV) can be identified in epithelium of a large proportion of patients with genital squamous lesions, relatively little is known about the extent of the local host immune response to this virus. We analyzed cervical secretions from patients undergoing evaluation because of abnormal Papanicolaou smears (cervical biopsy showed nonspecific atypia, flat condyloma, or intraepithelial neoplasia), as well as controls, for immunoglobulin binding to proteins produced in vitro to HPV -16 L1, E4, and E7 open reading frames. Segments of the HPV -16 genome, including portions of the L1 (nucleotides 6153-6794), E4 (nucleotides 3399-3648), and E7 (nucleotides 686-880) open reading frames, were cloned into pATH vectors and expressed as tryptophan synthetase E fusion proteins in Escherichia coli and used as a source of study antigens. Fusion proteins containing the HPV L1, E4, and E7 polypeptides were found to be distinct by molecular weight (59,000; 45,000; and 42,000) as well as by immunological determinants recognized by heterologous immune sera. Of 8 cervical intraepithelial neoplasia lesions tested by RNA-RNA in situ hybridization, 7 were found to be positive for HPV -16-related nucleic acids, in contrast to none (0 of 4) in the condyloma group (three positive for HPV DNA other than type 16). Immunoglobulin in cervical secretions showed reactivity to HPV type 16 E4 or L1 or both, with highest binding in patients with cervical intraepithelial neoplasia (P less than 0.01 for HPV -16 L1 and E4 compared with controls). Binding was not tryptophan synthetase E dependent and was, in general, coincident for the HPV -16 E4 and L1 proteins. We conclude that study of cervical secretions, using a quantitative assay for immunoglobulin binding to HPV -16 proteins produced in vitro, may be useful to document the quality and quantity of the immune response of the host to this important human pathogen.

7/AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06630287 90347836

Prevalence of antibodies to human papillomavirus type 8 in human sera.

Steger G; Olszewsky M; Stockfleth E; Pfister H

Institut fur Klinische und Molekulare Virologie, Friedrich-Alexander Universitat, Erlangen, Federal Republic of Germany.

Journal of virology (UNITED STATES) Sep 1990, 64 (9) p4399-406, ISSN 0022-538X Journal Code: KCV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The epidermodysplasia verruciformis-associated human papillomavirus type 8 (HPV -8) poses a high risk for malignant conversion of skin lesions in patients with epidermodysplasia verruciformis. For seroepidemiological studies, the HPV -8 open reading frames for E1, E2, E4, E6, E7, and L1 were bacterially expressed as beta-galactosidase fusion proteins , which were purified by preparative gel electrophoresis. Cleavage with the protease FXa at the engineered recognition site separated the beta-galactosidase polypeptide part from the viral polypeptide. Western blot analysis of 445 serum samples from a randomly selected population with the entire L1 as antigen revealed HPV -8-specific immunoglobulin G antibodies in 20% of the samples. The percentage of positive sera did not significantly differ in different age groups. In some sera, we could also detect immunoglobulin M antibodies. The use of two shortened L1 polypeptides as antigen indicated that there are at least two reactive epitopes in the case of HPV -8 L1. Several sera contained antibodies to the early proteins E1, E2, E4, and E7. E1 and E7 were predominantly detected by sera which were negative for L1. In one case, we found

antibodies to E6. Two of four sera of patients with epidermodysplasia verruciformis reacted with HPV -8 L1. The prevalence of anti-HPV -8-L1 antibodies in patients with malignant melanomas was comparable to that in the normal population (27.8%) but was significantly higher in patients with cervical cancer (37.5%), basaliomas (40%), and squamous cell skin carcinomas (72.7%) and in immunocompromised patients with Hodgkin's disease (47.7%).

7/AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06620796 90156517
An antigen chimera of poliovirus induces antibodies against human papillomavirus type 16.
Jenkins O; Cason J; Burke KL; Lunney D; Gillen A; Patel D; McCance DJ; Almond JW
United Medical School, University of Reading, United Kingdom.
Journal of virology (UNITED STATES) Mar 1990, 64 (3) p1201-6, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
It has been established that the surface of poliovirus type 1 can be extensively modified to incorporate antigenic domains from other poliovirus serotypes and from unrelated viruses. The fact that the modified (chimeric) viruses exhibit dual antigenicity and immunogenicity led us to explore the possibility of using the Sabin vaccine strain of poliovirus type 1 as a vector for the presentation of antigenic domains from human papillomavirus type 16 (HPV -16), a virus associated with the development of cervical carcinoma . We report here the construction and characterization of a chimeric poliovirus containing a 16-residue sequence derived from the major capsid protein (L1) of HPV -16. This virus chimera stimulated the production in rabbits of antibodies which recognized the HPV -16-derived peptide and an L1 fusion protein synthesized in Escherichia coli and detected HPV -16 in human biopsy material by immunoperoxidase staining. The possibility that poliovirus-HPV chimeras could be used as vaccines against HPV -16 is discussed.

7/AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06073067 88219535
Detection of human papillomavirus capsid antigens in various squamous epithelial lesions using antibodies directed against the L1 and L2 open reading frames.
Firzlaff JM; Kiviat NB; Beckmann AM; Jenison SA; Galloway DA
Fred Hutchinson Cancer Research Center, Seattle, Washington 98104.
Virology (UNITED STATES) Jun 1988, 164 (2) p467-77, ISSN 0042-6822 Journal Code: XEA
Contract/Grant No.: PO1-CA42792, CA, NCI; RO1-CA35568, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
HPV6 and HPV16 infect the squamous epithelium of the genital tract and are thought to be involved in the pathogenesis of benign and malignant lesions. HPV6 is primarily found in benign condylomas whereas HPV16 is present in dysplasias and in invasive squamous cell carcinomas . To examine the expression of the major and minor capsid proteins in these lesions polyclonal antisera directed against bacterially derived fusion

proteins harboring different restriction fragments of the L1 and L2 ORFs of HPV6b and HPV16 were generated. L1 ORF-specific antisera were not type-specific and detected the major capsid antigen in lesions infected with related HPV types. Anti-L2 ORF antisera could distinguish among HPV1 , HPV6 , and HPV16 when the fusion protein used as the immunogen did not harbor the amino-terminus of the L2 ORF. The anti-L1 ORF antisera were employed to detect the major capsid protein in various lesions by immunohistochemical staining. Lesions harboring HPV16 were positive in a high percentage of cervical intraepithelial neoplasia I-II (87%), and less frequently in carcinomas in situ (29%) or invasive carcinomas (17%). In all cases capsid antigen expression was restricted to cells showing some differentiation at the surface or periphery of the lesion.

7/AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06072785 88215042
Identification of immunoreactive antigens of human papillomavirus type 6b by using Escherichia coli-expressed fusion proteins.
Jenison SA; Firzlaff JM; Langenberg A; Galloway DA
Fred Hutchinson Cancer Research Center, Seattle, Washington 98104.
Journal of virology (UNITED STATES) Jun 1988, 62 (6) p2115-23, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: PO1-CA42792, CA, NCI; RO1 CA35568, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Human papillomavirus (HPVs) infect the genital epithelium and are found in proliferative lesions ranging from benign condylomata to invasive carcinomas . The immunological response to these infections is poorly understood because of the lack of purified viral antigens. In this study, bacterially derived fusion proteins expressing segments of all the major open reading frames (ORFs) of HPV type 6b (HPV -6b) have been used in Western blot (immunoblot) assays to detect antibodies directed against HPV -encoded proteins. The most striking reactivities present in sera from patients with genital warts were to the HPV -6b L1 ORF protein and, to a lesser extent, to the HPV -6b L2 ORF protein. Two cases of reactivity to HPV -6b E2 ORF were observed, but no reactivities were seen with other HPV -6b constructs. Two sera reacted with the HPV -16 L2 fusion protein , and two sera reacted with the HPV -16 E4 protein. The antibodies directed against the HPV -6b fusion proteins showed no cross-reactivity with comparable regions of the HPV -16 ORFs. This assay provides a useful approach for further studies of HPV serology.

7/AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05764014 89279201
Reactivities of polyclonal and monoclonal antibodies raised to the major capsid protein of human papillomavirus type 16.
Patel D; Shepherd PS; Naylor JA; McCance DJ
Department of Microbiology, United Medical School Guy's Hospital, London, U.K.
Journal of general virology (ENGLAND) Jan 1989, 70 (Pt 1) p69-77, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Polyclonal and monoclonal antibodies have been raised against a fusion protein containing beta-galactosidase and part of the major capsid protein L1 of the human papillomavirus (HPV) type 16. The polyclonal antibodies cross-reacted with the L1 protein of several HPV types including HPV -1, -2, -6 and -11 when reacted with virus-infected tissue sections, and with HPV -6 and -18 L1 fusion proteins on Western blotting. Monoclonal antibodies against the L1 fusion protein of HPV -16 reacted only with HPV -16 L1 fusion proteins on Western blots and with HPV -16-containing biopsy sections as assessed by in situ DNA-DNA hybridization. These antibodies did not detect HPV -6 L1 protein after Western blotting or in HPV -6-infected tissue sections, although one did react with an HPV -18 fusion protein after Western blotting. The monoclonal antibodies were able to detect HPV -16 antigens in routine formaldehyde-fixed, wax-embedded sections of cervical intraepithelial neoplasia sections. HPV -16 L1 proteins were seen in one-third of biopsies that were positive using the polyclonal cross-reacting antisera. Polyclonal antibodies to fusion proteins containing part of the minor capsid protein L2 of HPV -6 or -16 appeared to be more type-specific as no cross-reactivity was seen when these antibodies were reacted with HPV -1- and -2-infected tissue sections.

7/AB/21 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08854650 BIOSIS NO.: 199396006151
Human papillomaviruses in premalignant lesions of genital squamous epithelia and in tumour-derived cell lines.
AUTHOR: Auvinen Eeva
AUTHOR ADDRESS: Dep. Virol. and Biochem., Univ. Turku, Turku**Finland

JOURNAL: Annales Universitatis Turkuensis Series A II Biologica-Geographica-Geologica 0 (80):p1-47 1992
ISSN: 0082-6979
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In this thesis several aspects of human papillomavirus infections were studied by methods of molecular biology. Different nucleic acid hybridization methods were tested for creating an optimal system for screening clinical specimens for the presence of HPV . Human papillomavirus types 6, 11, 16, 18, 31 and 33 were studied. One question studied was the applicability of genital smear specimens compared to biopsy specimens for the dot blot nucleic acid hybridization test. Smear specimens are easier to take and prepare, and they are more practical in large scale screening tests for the presence of HPV . Smear specimens were found to be positive for HPV 6, 11, 16 or 18 with the same frequency as biopsy specimens from the same patients. However, as one of the specimens may give a negative result, testing of both specimens will increase the number of positive diagnoses. Further, different hybridization conditions were tested in the typing of HPV by dot blot hybridization. A high formamide concentration for achieving high stringency, a high SDS concentration for diminishing the background, and the addition of a polymer, such as polyethylene glycol, were found to be optimal for high specificity and relatively high sensitivity of the reaction. These conditions were used for the typing of a large number of HPV specimens. Flatbet scintillation counting was tested in the rapid quantitation of hybridization results. For HPV specimens, nucleic acid is at present the only applicable method for identification of an

infection. Scintillation counting thus offers an alternative for quantitative measurement of the hybridization signal. However, there are some problems, such as the nonspecific binding of radioactive material on the membrane, which cannot be avoided in routine practice, and which will result in false positive interpretations. The gene expression of the main oncogenic HPV type, HPV 16, was further studied in genital premalignant lesions. Expression of one of the capsid protein, L2, was studied at the mRNA level by in situ hybridization with single-stranded RNA probes. For studying gene expression at the protein level, a fragment from the L2 gene was cloned into a bacterial expression vector and production of the fusion protein was induced. The protein was purified and used for raising antibodies in rabbits. These antibodies were used to study the protein expression in human tissue material by immunohistochemical staining. Expression of the L2 gene was observed in condylomas and in dysplasias in the middle and upper layers of the epithelium. Expression of the E7 gene, an early gene with oncogenic potential, was studied at the mRNA level. It was mainly expressed in the middle and upper layers of the dysplastic epithelia. The expression of both genes seemed to be increased with higher grade of dysplasia. To better understand the role of HPV in the development of dysplastic lesions of genital squamous epithelia and in continuous cell growth in vitro, two cell lines were derived from vaginal premalignant lesions. The original lesions were positive for HPV 33 and HPV 16, respectively. In the HPV 33 positive cell line, the originally episomal HPV 33 DNA was probably integrated into the cellular DNA during early cell passaging, and was undetectable in the later passages. Either it was present in only a small population of cells, or was absent altogether. Since the cells grow continuously, it is tempting to speculate that HPV has caused the continuous cell growth but is not necessary for the maintenance of immortalization. For the HPV 16 containing cells, an abnormal restriction, and in the cells HPV 16 has been detected only with PCR. It is possible that HPV 16 DNA is present in only a small population of cells. In this thesis both the presence of HPV DNA and the expression of mRNA and protein in natural lesions was studied. Since papillomaviruses do not grow in culture, the only material available for HPV studies are natural lesions and cell lines, either derived from natural tissue or constructed by transfection. Further studies on this material may reveal new aspects of papillomavirus infections in humans.

1992

7/AB/22 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07421502 BIOSIS NO.: 000091027491
IDENTIFICATION OF SEROREACTIVE REGIONS OF THE HUMAN PAPILLOMAVIRUS TYPE 16 PROTEINS E4 E6 E7 AND L1
AUTHOR: MUELLER M; GAUSEPOHL H; DE MARTYNOFF G; FRANK R; BRASSEUR R; GISSMANN L
AUTHOR ADDRESS: DEUTSCHES KREBSFORSCHUNGSZENTRUM, IM NEUENHEIMER FELD 280, 6900 HEIDELBERG.
JOURNAL: J GEN VIROL 71 (11). 1990. 2709-2718. 1990
FULL JOURNAL NAME: Journal of General Virology
CODEN: JGVIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Small fragments of the DNA of human papillomavirus type 16 (HPV -16) were randomly cloned into the bacteriophage fd which expresses

the resulting peptides as part of its capsid . Antisera raised against different HPV -16 fusion proteins were used for screening of the phage clones and the reacting peptides were determined by sequencing the inserted HPV -16 DNA fragments of the positive recombinants. Seroreactive regions of the proteins derived from the E4, E6, E7 (two regions) and L1 (three regions) open reading frames could be found by this approach. Of this approach. Of these seven regions, four were defined by at least two overlapping inserts, thus limiting the domains to between 10 and 15 amino acids. In the case of the E4 open reading frame, the same region identified by immunoscreening was also found when synthetic overlapping octapeptides were tested by ELISA with the anti-E4 antiserum. Using an approach to predict 'receptor-like' regions within the respective proteins, five of the seven regions were also identified. From the data on these regions, synthetic peptides were produced and used for the detection of antibodies against HPV -16 proteins in human sera by ELISA.

1990

7/AB/23 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06992275 BIOSIS NO.: 000089093539
AN ANTIGEN CHIMERA OF POLIOVIRUS INDUCES ANTIBODIES AGAINST HUMAN PAPILLOMAVIRUS TYPE 16
AUTHOR: OWEN J; CASON J; BURKE K L; LUNNEY D; GILLEN A; PATEL D; MCCANCE D J; ALMOND J W
AUTHOR ADDRESS: UNITED MED. DENTAL SCH. DEP. MICROBIOL., UNIV. READING, LONDON RD., READING RG1 5AQ.
JOURNAL: J VIROL 64 (3). 1990. 1201-1206. 1990
FULL JOURNAL NAME: Journal of Virology
CODEN: JOVIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: It has been established that the surface of poliovirus type 1 can be extensively modified to incorporate antigenic domains from other poliovirus serotypes and from unrelated viruses. The fact that the modified (chimeric) viruses exhibit dual antigenicity and immunogenicity led us to explore the possibility of using the Sabin vaccine strain of poliovirus type 1 as a vector for the presentation of antigenic domains from human papillomiavirus type 16 (HPV -16), a virus associated with the development of cervical carcinoma . We report here the construction and characterization of a chimeric poliovirus containing a 16-residue sequence derived from the major capsid protein (L1) of HPV -16. This virus chimera stimulated the production in rabbits of antibodies which recognized the HPV -16-derived peptide and an L1 fusion protein synthesized in Escherichia coli and detected HPV -16 in human biopsy material by immunoperoxidase staining. The possibility that poliovirus-HPV chimeras could be used as vaccines against HPV -16 is discussed.

1990

7/AB/24 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04213509 Genuine Article#: RN779 Number of References: 31
Title: LEUKOCYTE PROLIFERATION IN-VITRO AGAINST COTTONTAIL RABBIT PAPILLOMAVIRUS IN RABBITS WITH PERSISTING PAPILLOMAS CANCER OR AFTER REGRESSION (Abstract Available)
Author(s): HOPFL R; CHRISTENSEN ND; ANGELL MG; KREIDER JW
Corporate Source: INNSBRUCK UNIV,DEPT DERMATOL & VENEROL,ANICHSTR35/A-6020 INNSBRUCK//AUSTRIA/; PENN STATE UNIV,MILTON S HERSHEY MED CTR,DEPT PATHOL/HERSHEY//PA/17033; PENN STATE UNIV,MILTON S HERSHEY MED CTR,DEPT MICROBIOL & IMMUNOL/HERSHEY//PA/17033
Journal: ARCHIVES OF DERMATOLOGICAL RESEARCH, 1995, V287, N7 (SEP), P 652-658
ISSN: 0340-3696
Language: ENGLISH Document Type: ARTICLE
Abstract: Leukocyte proliferation responses to cottontail rabbit papillomavirus (CRPV) were measured in vitro with fresh whole blood as well as with ammonium chloride lysis-separated leukocytes. The antigens used were (1) CRPV particles produced in the athymic (nu/nu) mouse xenograft system and (2) purified bacterial fusion proteins of the CRPV major and minor capsid proteins L1 and L2. CRPV-infected domestic rabbits with persistent papillomas or after papilloma regression, as well as uninfected controls were studied. There was a clearcut difference between infected and uninfected animals. We demonstrated antigen-specific leukocyte proliferation to at least one CRPV antigen in 12 of 21 infected rabbits but there was no positivity in 9 control animals (P = 0.004). There was whole-blood reactivity preferentially to intact CRPV particles in regressors, Specific but weak leukocyte proliferation against CRPV particles was detected in 6 of 9 regressor rabbits (66%) but only in 1 of 12 progressors (8%; P = 0.0158). This trend of greater reactivity to intact CRPV particles in regressors as compared with progressors was not seen with peripheral blood leukocytes isolated by ammonium chloride lysis. We conclude that specific leukoproliferative responses against capsid CRPV proteins exist in rabbits experimentally infected with CRPV.

7/AB/25 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02658663 Genuine Article#: LU337 Number of References: 15
Title: SEQUENCE AND ANTIGENIC DIVERSITY IN 2 IMMUNODOMINANT REGIONS OF THE L2-PROTEIN OF HUMAN PAPILLOMAVIRUS TYPE-6 AND TYPE-16 (Abstract Available)
Author(s): YAEGASHI N; XI LF; BATRA M; GALLOWAY DA
Corporate Source: FRED HUTCHINSON CANC RES CTR,1124 COLUMBIA ST/SEATTLE//WA/98104; FRED HUTCHINSON CANC RES CTR,1124 COLUMBIA ST/SEATTLE//WA/98104; UNIV WASHINGTON,DEPT PATHOL/SEATTLE//WA/98195; UNIV WASHINGTON,DEPT EPIDEMIOL/SEATTLE//WA/98195
Journal: JOURNAL OF INFECTIOUS DISEASES, 1993, V168, N3 (SEP), P743-747
ISSN: 0022-1899
Language: ENGLISH Document Type: NOTE
Abstract: To assess the extent of sequence and antigenic diversity in the minor capsid proteins (L2) of human papillomavirus (HPV) types 6 and 16, 24 clinical samples were obtained, and the regions encoding the immunodominant epitopes 6U3 and 16REx were amplified by polymerase chain reaction, sequenced, cloned into pATH plasmids, and tested for reactivity with human sera. Two of 11 HPV -6 DNAs were identical to the prototype strain in the 6U3 region, while 9 variants had a G to A transition at nt5020, changing a valine residue to isoleucine. Of 16 sera that did not react with the prototype HPV -6 L2 fusion protein , 2 reacted with the 6U3-isoleucine variant, and all 8 sera that

reacted with the prototype also reacted with the variant. Twelve of 13 HPV -16 DNAs were identical to the prototype strain in the 16REx region, while 1 variant had a C to G transversion at nt4825, changing a proline to an arginine, but not affecting antigenicity.

7/AB/26 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02602780 Genuine Article#: LP725 Number of References: 40
Title: RELATION BETWEEN SKIN- CANCER, HUMORAL RESPONSES TO HUMAN PAPILLOMAVIRUSES, AND HLA CLASS-II MOLECULES IN RENAL-TRANSPLANT RECIPIENTS (Abstract Available)
Author(s): BAVINCK JNB; GISSMANN L; CLAAS FHJ; VANDERWOUDE FJ; PERSIJN GG; TERSCHEGGET J; VERMEER BJ; JOCHMUS I; MULLER M; STEGER G; GEBERT S; PFISTER H
Corporate Source: LEIDEN UNIV HOSP,DEPT DERMATOL,RIJNSBURGERWEG 10/2333 AA LEIDEN//NETHERLANDS/; LEIDEN UNIV HOSP,DEPT IMMUNOHEMATOL/2333 AA LEIDEN//NETHERLANDS/; LEIDEN UNIV HOSP,BLOOD BANK/2333 AA LEIDEN//NETHERLANDS/; LEIDEN UNIV HOSP,DEPT NEPHROL/2333 AA LEIDEN//NETHERLANDS/; EUROTRANSPLANT FDN/LEIDEN//NETHERLANDS/; UNIV AMSTERDAM,ACAD MED CTR,DEPT VIROL/1105 AZ AMSTERDAM//NETHERLANDS/; GERMAN CANC RES CTR/W-6900 HEIDELBERG 1//GERMANY/; UNIV ERLANGEN NURNBERG,INST KLIN & MOLEK VIROL/W-8520 ERLANGEN//GERMANY/
Journal: JOURNAL OF IMMUNOLOGY, 1993, V151, N3 (AUG 1), P1579-1586
ISSN: 0022-1767
Language: ENGLISH Document Type: ARTICLE
Abstract: Human papillomaviruses (HPV), especially the epidermodysplasia verruciformis (EV)-associated HPV 5, 8, 14, 17, 20, and 47, are thought to play a role in the pathogenesis of some skin cancers in recipients of renal allografts. MHC class I and class II genes are involved in the cellular immune response to viral and tumor Ag. Little is known about humoral responses to HPV in recipients with and without skin cancer . We investigated the prevalance of antibodies to the early (E) protein E7 and the major capsid late (L) protein L1 of HPV 8. In addition, we studied the association of HLA class II molecules with these antibody responses. The E7 and L1 open reading frames of HPV 8 were bacterially expressed as beta-galactosidase fusion proteins , which were purified by preparative gel electrophoresis. Serum samples from 36 renal transplant recipients with and 91 recipients without skin cancer were screened for the presence of IgG and IgM antibodies to HPV 8 E7 and L1, by Western blot analysis. The detection of anti-HPV 8 L1 antibodies represents the immune response to HPV 8 and possibly other EV-associated HPV , because cross-reactivity between the representatives of this HPV subgenus can occur. The antibody responses to HLA Ag were used as controls. Recipients who had IgM antibodies but no IgG antibodies to L1 of HPV 8 (patients with no apparent class switch from IgM to IgG) had skin cancer in 50% of cases, whereas recipients who produced IgG antibodies (patients with an apparently good humoral response to L1 of HPV 8) had skin cancer in only 18% of cases. The estimated relative risk of skin cancer in recipients with no class switch, compared with the risk in those with a good humoral response, was 4.5 (95% confidence interval, 1.1 to 18.1). We found no association between the antibody response to HLAAg and the occurrence of skin cancer . A strong linkage between the absent class switch of antibody production in response to L1 of HPV 8 and HLA-DR7 was observed (relative risk, 26.2). Renal transplant recipients who have no apparent class switch from IgM to IgG production in response to Ag encoded by L1 of HPV 8 or possibly other EV-associated HPV are at an increased risk of skin cancer . The

association with HLA-DR7 indicates a genetic control of skin cancer development or regression, involving genes in the class II region of the MHC.

7/AB/27 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01576174 Genuine Article#: HJ504 Number of References: 40
Title: HUMAN-ANTIBODIES RECOGNIZE MULTIPLE DISTINCT TYPE-SPECIFIC AND CROSS-REACTIVE REGIONS OF THE MINOR CAPSID PROTEINS OF HUMAN PAPILLOMAVIRUS TYPE-6 AND TYPE-11 (Abstract Available)
Author(s): YAEGASHI N; JENISON SA; BATRA M; GALLOWAY DA
Corporate Source: FRED HUTCHINSON CANC RES CTR/SEATTLE//WA/98104; FRED HUTCHINSON CANC RES CTR/SEATTLE//WA/98104; UNIV WASHINGTON,DEPT PATHOL/SEATTLE//WA/98195
Journal: JOURNAL OF VIROLOGY, 1992, V66, N4 (APR), P2008-2019
Language: ENGLISH Document Type: ARTICLE
Abstract: Human serum samples derived from a case-control study of patients with cervical carcinoma (n = 174) or condyloma acuminatum (n = 25) were tested for the presence of immunoglobulin G antibodies to human papillomavirus type 6 (HPV6) L2 and HPV11 L2 recombinant proteins in a Western immunoblot assay. Thirty-six samples (18%) were positive for HPV6 L2 antibodies alone, 25 (13%) were positive for HPV11 L2 antibodies alone, and 34 (17%) were positive for both HPV6 L2 and HPV11 L2 antibodies. Thirty samples that were positive for both antibodies were tested for the presence of HPV6 -HPV11 L2 cross-reactive antibodies. Fifteen (50%) serum samples contained HPV6 -HPV11 L2 cross-reactive antibodies, and 15 (50%) contained independent, type-specific HPV6 L2 and HPV11 L2 antibodies. Altogether, 82% of the HPV6 L2 and HPV11 L2 antibody reactivities were type specific and 18% were HPV6 -HPV11 cross-reactive. There was no significant difference in the prevalence of antibody reactivities between samples from patients with cervical carcinoma and those with condyloma acuminatum. Deletion mapping identified five HPV6 L2 regions that reacted with HPV6 type-specific antibodies: 6U1 (amino acids [aa] 152 to 173), 6U2 (aa 175 to 191), 6U3 (aa 187 to 199), 6U4 (aa 201 to 217), and 6U5 (aa 351 to 367). Five HPV11 L2 regions that reacted with HPV11 type-specific antibodies were identified: 11U1 (aa 49 to 84), 11U2 (aa 147 to 162), 11U3 (aa 179 to 188), 11U4 (aa 180 to 200), and 11U5 (aa 355 to 367). Two HPV6 - HPV11 cross-reactive regions were identified: 6CR1 (HPV6 L2 aa 106 to 128)/11CR1 (HPV11 L2 aa 103 to 127) and 6CR2 (HPV6 L2 aa 187 to 199)/11CR2 (HPV11 L2 aa 180 to 200).

7/AB/28 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01332175 Genuine Article#: GP878 Number of References: 41
Title: ANTIGENIC AND IMMUNOGENIC EPITOPES SHARED BY HUMAN PAPILLOMAVIRUS TYPE-16 AND BOVINE, CANINE, AND AVIAN PAPILLOMAVIRUSES (Abstract Available)
Author(s): DILLNER L; HEINO P; MORENOLOPEZ J; DILLNER J
Corporate Source: KAROLINSKA INST,DEPT VIROL/S-10521 STOCKHOLM//SWEDEN/; KAROLINSKA INST,DEPT VIROL/S-10521 STOCKHOLM//SWEDEN/; BIOMED CTR,DEPT VET MICROBIOL/S-75123 UPPSALA//SWEDEN/
Journal: JOURNAL OF VIROLOGY, 1991, V65, N12, P6862-6871
Language: ENGLISH Document Type: ARTICLE

Abstract: All types of papillomaviruses (PV) share common, so-called group-specific epitopes. To identify the major group-specific epitopes, we immunized 26 guinea pigs or rabbits with purified bovine PV type 1 (BPV), canine PV, or avian PV from the common chaffinch. The resulting hyperimmune sera, as well as a commercially available rabbit antiserum to BPV and seven monoclonal antibodies to BPV, were tested in an enzyme-linked immunosorbent assay with a set of 66 overlapping 20-amino-acid peptides representing the complete sequence of the major capsid proteins (L1 and L2) of human PV type 16 (HPV 16). Sera from the same animals before immunization were used as controls. The minimal reactive epitopes within each peptide were further characterized by testing of truncated peptides. The cross-reactive epitopes were clustered in two regions of L1, an internal region (at positions 171 to 235), which contained three epitopes, and the more reactive region at the carboxy terminus (at positions 411 to 475), which contained six epitopes. The most reactive of the HPV 16 broadly cross-reactive epitopes was a carboxy-terminal epitope which had the sequence DTYRF and which reacted with nine of the antisera to BPV, canine PV, or avian PV, with the commercially available rabbit antiserum to BPV, and also with a mouse monoclonal antibody to BPV. Antipeptide antisera to all of the HPV 16 L1 peptides and to the most antigenically reactive of their truncated analogs were made in guinea pigs. Antipeptide antisera reactive with BPV were obtained for three of the cross-reactive epitopes, and one of these antisera allowed highly sensitive detection of group-specific PV antigen by immunoperoxidase staining.

1080225 AAD8923652
IMMUNOLOGIC CHARACTERIZATION OF HUMAN PAPILLOMAVIRUS TYPE 16
Author: BEISS, BARBARA K.
Degree: PH.D.
Year: 1989
Corporate Source/Institution: YESHIVA UNIVERSITY (0266)
Source: VOLUME 50/07-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
PAGE 2831. 275 PAGES

Papillomaviruses (PV) are small DNA viruses which infect human and animal species, and are associated with benign and malignant proliferative lesions. Human papillomaviruses (HPV) are etiologically associated with the development of cervical cancer . Peptides from the carboxyterminus of HPV -16 L1 and L2 open reading frames (ORF)s, selected on the basis of hydrophilicity and secondary structure, were synthesized and used to generate high titered polyclonal and monoclonal anti-peptide sera. The HPV type specificity of these anti-peptide sera was determined by Western blot analysis using a panel of recombinant HPV proteins. Antisera to a HPV -16 L1 carboxyterminal peptide reacted specifically with L1 fusion proteins from HPV -16, but not with HPVs -1, -6, -11, -18, or BPV-1 or -2. Antisera to a HPV -16 L2 carboxyterminal peptide reacted with L2 proteins from HPV -16 and HPV -6, but not BPV-1. Computer analysis of carboxyterminal amino acid sequences of PV L1 proteins showed no significant homology between HPV -16 L1 and L1 proteins of other HPV types or BPV. In contrast, there was considerable similarity between carboxyterminal amino acid sequences of HPV -16 L2 and L2 proteins of other genital HPV , but not nongenital HPV or BPV. Antisera to the HPV -16 L1 peptide recognized nuclear antigen(s) in formal in-fixed, paraffin embedded cervical lesions infected with several genital HPV

types, including HPV -16, 11, and 18, using immunoperoxidase techniques. Anti-L2 peptide sera did not react with capsid proteins in tissues. In addition, anti-16 L1 peptide serum immunoprecipitated an HPV -16 L1 recombinant protein, but not BPV-L2 proteins. Thus, antisera to carboxyterminal amino acids in HPV -16 major capsid proteins identified an HPV -16 type specific linear epitope in the L1 protein and a partially type-common epitope(s) in the L2 protein.

We have demonstrated antibodies reactive with bovine papillomavirus (BPV) virions in sera of many HPV -infected patients. We were unable to detect serologic responses to several HPV -16 L1 and L2 synthetic peptides. Preliminary data shows few humoral immune responses to HPV L1 recombinant proteins expressed in bacteria, but not to early PV proteins. The specificity of these responses has not been delineated.

7/AB/30 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10727453 EMBASE No: 2000136809
Construction of a recombinant adenovirus vector of human papillomavirus type 16 L1-E7C

Bian J.-F.; Yu X.-P.; Wang Y.; Zhao W.-M.; Zhang L.-H.; Dong J.-D.; Jia J.- H.; Zhou Y.-B.; Luan Y.; Qi M.; Chen H.-B.
X.-P. Yu, Laboratory of Molecular Biology, Department of Microbiology, Shandong Medical University, No. 44, Wenhua West Road, Ji'nan 250012 China
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Chinese Journal of Cancer Research (CHIN. J. CANCER RES.) (China) 2000, 12/1 (21-24)
CODEN: CJCRF ISSN: 1000-9604
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 16

Objective: Human papillomaviruses are closely associated with human cervical cancer , especially HPV types 16 and 18. At present, HPV can not be produced in large quantity; it also has tumorgenicity and these properties of HPV have seriously hampered the development of HPV vaccine. HPV type 16 L1 proteins can assembled into virus-like particles (VLP), which are morphologically identical to the nature virion. In order to develop the recombinant adenovirus vectors of HPV , we constructed a recombinant adenovirus shuttle plasmid pCA14 L1-E7C. Methods: Human papillomavirus type 16 L1 open reading frame without terminator codon (TAA) (5559-7152) and E7C (682-855) were amplified using PCR. The L1 and E7C fragments were inserted into pGEM-T easy vectors by T-A strategy, named pTAL1 and pTAE7C. pTAL1 was cut with Hind III and BgIII, the pTAE7C with BamHI and ClaI. The L1 DNA fragment, E7C and pBluesscript SK were ligated together using T4 DNA ligase. pBSL1-E7C and pBSL1-E7C was digested with Hind III and Xhol. The L1-E7C fragment was inserted into adenovirus shuttle plasmids pCA14, named pCA14L1- E7C. DNA sequence results indicated that The L1-E7C DNA fragment can encode the HPV16L1 -E7 fusion protein correctly. Results: The L1 and E7C DNA fragments were amplified by PCR and recombinant plasmid pTAL1, pTAE7C, pBSL1- E7C and pCA14L1-E7C were constructed correctly. The pCA14L1-E7C can be used in the further research work, cotransfected the 293 cell with the parent adenovirus pBHG10. Conclusion: Our results indicated that we have constructed a HPV16L1 -E7 fusion DNA fragments and the adenovirus shuttle plasmids pCAL1- E7C for the further research.

7/AB/31 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01966592 SUPPLIER NUMBER: 69371771 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Papillomavirus-Like Particle Vaccines.
Schiller, John T.; Lowy, Douglas R.
Journal of the National Cancer Institute, 50
Dec 30,
2000
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0027-8874
LANGUAGE: English RECORD TYPE: Abstract TARGET AUDIENCE: Professional

AUTHOR ABSTRACT: Papillomavirus -like particle (VLP)-based subunit vaccines have undergone rapid development over the past 8 years. Three types are being investigated. The most basic type is composed of only the L1 major capsid protein and is designed to prevent genital human papillomavirus (HPV) infection by inducing virus-neutralizing antibodies. On the basis of positive results in animal models, clinical trials of this type of vaccine for HPV16 , and other types, are currently under way. Preliminary results have been encouraging in that systemic immunization with the L1 VLPs induced high serum titers of neutralizing antibodies without substantial adverse effects. The second type of vaccine incorporates other papillomavirus polypeptides into the VLPs as L1 or L2 fusion proteins . These chimeric VLPs are designed to increase the therapeutic potential of an HPV vaccine by inducing cell-mediated responses to nonstructural viral proteins, such as E7. Studies in mice indicate that these vaccines generate potent antitumor cytotoxic lymphocyte (CTL) responses while retaining the ability to induce high-titer neutralizing antibodies. It is likely that prophylactic and therapeutic clinical trials of chimeric VLPs will be initiated in the near future. The third type of VLP-based vaccine is designed to induce autoantibodies against central self-antigens by incorporating self-peptides into the outer surface of VLPs, a process that could have therapeutic potential in various disease settings unrelated to HPV infection. In a recent proof of concept study, a peptide from an external loop of mouse CCR5 protein was inserted into a neutralizing epitope of L1. In mice, the particles generated by this chimeric L1 were able to induce high titers of CCR5 antibodies that specifically recognized the surface of CCR5-transfected cells and blocked in vitro infection of an M-tropic human immunodeficiency virus strain. (J Natl Cancer Inst Monogr 2000;28: 50-4)

7/AB/32 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01955497 SUPPLIER NUMBER: 67881093 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Spontaneous regression of CIN and delayed-type hypersensitivity to HPV-16 oncoprotein E7.(Commentary)
Hopfl, Reinhard; Heim, Kurt; Christensen, Neil; Zumbach, Klaus; Wieland, Ulrike; Volgger, Birgit; Widschwendter, Andreas; Haimbuchner, Sandra; Muller-Holzner, Elisabeth; Pawlita, Michael; Pfister, Herbert; Fritsch, Peter
The Lancet, 356, 9246, 1985
Dec 9,
2000
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0099-5355
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 1521 LINE COUNT: 00171

7/AB/33 (Item 3 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01609314 SUPPLIER NUMBER: 17989078 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Serum antibody to HPV-16 VLPs indicates cervical HPV-16 infection.(human papillomavirus type 16, virus-like particles)
Clark, Cathy
Cancer Biotechnology Weekly, p9(2)
Dec 25,
1995
PUBLICATION FORMAT: Magazine/Journal LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 617 LINE COUNT: 00056

7/AB/34 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0148812 DBA Accession No.: 93-06864
Towards vaccines against human papilloma virus type-16 genital infections- recombinant vaccine production for cervix carcinoma prevention; a review
AUTHOR: Cason J; Khan S A; Best J M
CORPORATE SOURCE: The Richard Dimbleby Laboratory of Cancer Virology, The Rayne Institute, St. Thomas's Campus, Lambeth Palace Road, London SE1 7EH, UK.
JOURNAL: Vaccine (11, 6, 603-11) 1993
CODEN: VACCDE
LANGUAGE: English
ABSTRACT: Strategies for recombinant vaccine production against human papilloma virus-16 (HPV -16) are reviewed, with respect to: cervix carcinoma ; papilloma virus infection (virology and immunology); intervention against HPV -16-associated cancers ; prevention of primary HPV -16 infection; and therapeutic vaccines. Bacterially-derived recombinant proteins are not post-transcriptionally modified, may mimic only linear epitopes, and the structure may be compromised if fusion proteins are used. Eukaryotically expressed recombinant proteins may be better imitations of native viral proteins, and thus more likely to induce neutralizing antibodies. Yeast and baculo virus expression systems have been used to produce non-fused HPV -16 capsid proteins which may be used as prophylactic vaccines against HPV -16. Virus-like particles of HPV -16 have been constructed using a vaccinia virus vector, for use as a live recombinant vaccine. However, neutralizing epitopes of HPV -16 particles have not yet been defined. (146 ref)
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